EFFECTS OF PSYCHOLOGICAL STRESS ON BLOOD GLUCOSE IN DIABETES

By

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A DISSERTATION PRESENTED TO THE GRADUATE SCHOOL
OF THE UNIVERSITY OF FLORIDA IN PARTIAL FULFILLMENT
OF THE REQUIREMENTS FOR THE DEGREE OF
DOCTOR OF PHILOSOPHY

UNIVERSITY OF FLORIDA

1990

ACKNOWLEDGEMENTS

I want to take this opportunity to acknowledge those people whose contributions were so important to the completion of this project. First and foremost, I wish to express my deepest appreciation and heartfelt gratitude to my chairperson, Dr. Suzanne B. Johnson, for her generous gift of personal time, professional guidance, and patience. Her excellent insights and suggestions were invaluable. She provided the best mixture of guidance and freedom for independence and was quick to step in when needed.

I would also like to thank the other members of my committee, Drs. Fred Murray, Neil Rowland, Janet Silverstein, Gary Geffken, Hugh Davis, and Jim Rodrigue, for their valuable suggestions, thoughts and ideas. I am particularly grateful to Dr. Fred Murray and Dr. Neil Rowland for their constructive feedback and reviews. Their suggestions, physiological expertise, and enthusiastic encouragement were vital to the completion of the project. Additionally, I thank Fred for providing the necessary medical backup and Neil for analyzing the plasma cortisol samples.

I owe special thanks to Lisa Sheeber for running the show in my absence. Her diligence and persistence are greatly appreciated. I want to thank the CRC staff for their assistance in the collection of these data and ongoing encouragement. Special thanks go to Michael Kelly who calmly addressed all my naive computer-related questions and concerns. I am very grateful to Sarah Connelly who stepped in at the last minute to perform the tedious job of preparing the final manuscript. Her patience and initiative are greatly appreciated.

I want to thank my wonderful parents who have always encouraged my dreams and endeavors and provided the consistent love, support, and confidence to make it all possible.

I want to thank my great friend Dave Saliwanchik whose loving support and generosity allowed me to be in a position to complete this project. I will always cherish his friendship.

I want to give very special thanks to Craig Lipman who has been a constant source of support and inspiration. His love, laughter, wisdom, and patience are priceless. I greatly appreciate the time and effort he willingly gave to this project. Without his programming genius the improved stress program would not have been available.

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August 1990

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Major Department: Clinical and Health Psychology

There is an increasing amount of evidence suggesting that psychological stress can cause metabolic derangements in diabetic patients. Laboratory stress-induction methods evaluating blood glucose reactivity have yielded mixed results, with blood glucose sometimes showing an increase, decrease, or no change. The methodological flaws present in most of these studies may contribute to the variability in findings. This investigation was designed to evaluate blood glucose reactivity to a psychological stressor (a challenging computer "game" that induces monetary losses) in subjects with insulin-dependent diabetes mellitus (IDDM) N =

9, noninsulin-dependent diabetes mellitus (NIDDM) N = 9, and nondiabetic controls N= 16. Groups were balanced for age, sex, and body mass index. Subjects participated in two separate morning sessions. At each session they arrived fasting. After a baseline period, they were given 8 oz of a mixed meal beverage (Sustacal). On nonstress days, subjects watched an educational video after the Sustacal; on stress days, they participated in the challenging computer task. Plasma glucose was measured on 10 occasions over each 120 minute session. Results of heart rate and self-report data confirmed that the stressor was arousing. Each group displayed different patterns in response to stress. In nondiabetic subjects, stress delayed the peak in the glucose curve. Subjects with NIDDM showed a relative increase in blood glucose during the stressor and a peak shift in the reverse direction from the nondiabetic subjects. Subjects with IDDM showed yet a different pattern with an initial decrease in blood glucose during the stressor followed by an increase. The results help to reconcile previous conflicting data on this subject.

CHAPTER 1
INTRODUCTION

Diabetes mellitus is characterized either by a defect in insulin secretion or inefficient use of available insulin by body tissues. Insulin has many metabolic functions including making cell membranes permeable to glucose. In diabetes, because of insufficient insulin production or inefficient insulin utilization, glucose cannot readily be used by the cells of the body; it accumulates in the bloodstream (hyperglycemia) and spills over into the urine (glycosuria). Because the cells cannot metabolize glucose, they instead metabolize fat and protein which results in high levels of fatty acids and ketones in the blood and urine. This process, if untreated, results in frequent urination (in an attempt to rid the body of excessive fatty acids), dehydration, fatigue, weight loss, and ketoacidosis, hyperosmolar coma, and death. With appropriate medical treatment, the consequences of severe hyperglycemia can be avoided and life prolonged. However, even moderately elevated blood glucose levels over a long period may be related to the eventual appearance of the long-term complications of diabetes (e.g., retinopathy, nephropathy, neuropathy, accelerated cardiovascular disease).

Two forms of diabetes are commonly identified: insulin-dependent diabetes mellitus (IDDM) and noninsulin-dependent diabetes mellitus (NIDDM). Insulin-dependent diabetes mellitus is also labeled juvenile onset diabetes or Type I diabetes because of its frequent advent during childhood. In this condition, the beta (or insulin-producing) cells of the pancreatic islets of Langerhans secrete little or no insulin. The patient, therefore, must continuously be treated with daily insulin injections. In contrast, patients with NIDDM, often labeled adult-onset diabetes or Type II diabetes, retain some beta cell function. However, high somatic resistance to insulin (often exacerbated by obesity) puts increased demands on the insulin-secretory capacity of these patients, who suffer from an inability to secrete enough insulin to meet these demands. Weight reduction, diet modification, or oral hypoglycemic agents that increase the effectiveness of endogenous insulin, can be used for treatment, although exogenous insulin replacement is sometimes needed by a few patients.

The long term complications associated with diabetes mellitus have been well documented. These complications include autonomic neuropathy, retinopathy, cardiovascular disease, kidney disease, blindness, impotence, peripheral vascular disease, and infection leading to gangrene. Recent findings, however, suggest that such complications are not

inevitable. Most investigators now agree that improved diabetic control (defined as the degree to which blood sugar levels are maintained within the normal range) is effective in reducing the occurrence and severity of both long and short term complications (Cahill, Etzwiler, & Freinkel, 1976; Davidson, 1981). Normoglycemia is, in fact, the principal therapeutic goal for patients with diabetes. To this end, insulin therapy must be regulated to meet the metabolic requirements associated with changes of diet, physical activity, and physical stress from such causes as infection, trauma, or other disease states.

There is some evidence that psychological stress, in addition to physical stress, can cause metabolic derangements. Although the exact role of psychological stress in diabetes has been rather elusive and controversial, the literature contains a good deal of support for the belief that elevated blood glucose can be directly related to perceived threat or stress (Menninger, 1935; Hinkle & Wolf, 1952; Sackett & Haynes, 1976; Kirkley, 1982). The investigations in this field date back to 1877 when Boehm and Hoffman (Greydanus & Hoffman, 1979) found that they could produce glycosuria in cats within half an hour after enraging them and by inflicting pain. Cannon, Shohl, and Wright (1911) produced the same result by simply immobilizing the animals, without inflicting pain. They also discovered that the level of glucose found in the urine

of these animals increased in direct proportion to the rage of the animal.

"Emotional glycosuria" (Menninger, 1935) in man has been reported in the literature since the early part of this century. Folin, Denis, and Smillie (1914) discussed two experiments involving second-year medical students and female college students where the stress of an examination resulted in transient glycosuria in 18% of the students.

Psychological stress has been an important theoretical construct used to account for both onset and course of diabetes. Onset theories assume that the individual is at-risk for diabetes, but that it takes some trauma or stress to hasten the occurrence of the disease. However, the research methodology for investigating such precipitating stressful events has been wholly retrospective in nature. These types of studies can never satisfactorily address this topic because the data are slanted by the interpretation of the patient and family as to why the disease developed.

While there may be some controversy as to whether psychological stress is involved in the etiology of diabetes, there is general agreement that stress may influence the course (metabolic control) of patients with the disease.

In one study, adult patients were asked whether or not psychological stress affected the control of their diabetes;

the majority perceived that stress was very influential (Cox, Taylor, Nowacek, Holley-Wilcox, Pohl, & Guthrow, 1984).

One of the earliest demonstrations of stress effects in diabetes was a case report by Hinkle and Wolf (1949) describing a 15 year old girl with a repeated history of diabetic ketoacidosis. The teenager had a very poor relationship with her mother, with many violent arguments. In a diary, the patient recorded these daily stressful events and her urine ketone test results. The patient's recording showed a striking relationship between the two.

Mechanisms By Which Stress May Affect Diabetic Control

The mechanisms by which stress influences diabetic metabolism have not been well elucidated. The following two mechanisms have been suggested and may coexist:

1. Emotional arousal in response to stress may lead to changed production of particular hormones (catecholamines, cortisol, growth hormone) that in turn influence glucose and fat metabolism.

2. Stressful experiences may lead to changed adherence behavior including those of diet management, exercise, and insulin monitoring.

These mechanisms will be discussed in detail.

Physiological Mechanisms

Stress causes the body to react by secreting hormones which activate the release of stored glucose thereby ensuring adequate supplies of energy for the central nervous system and other body tissues, enabling the individual to fight or flee. Theoretically, exposure to stress is thought to have a significant effect on diabetic control through the effects of increased levels of the stress hormones--e.g. epinephrine, norepinephrine, cortisol. These hormones, when released into the blood in sufficient amounts, stimulate a complex series of events which may induce both hyperglycemia and excess ketone body production. Catecholamines antagonize the peripheral metabolic effects of insulin and stimulate glycogenolysis and gluconeogenesis by the liver, which should result in increased blood glucose levels in the patients with diabetes. Catecholamines also encourage mobilization of free fatty acids which are converted by the liver to ketone bodies. Ketone body production may lead to diabetic ketoacidosis in diabetes.

Once the stress terminates, there is typically a temporary exaggerated increase in insulin production--the normal function counters the stress hormones and permits the body to return to a normal metabolic state. Individuals with insulin dependent diabetes, whose pancreatic islets are unable to produce normal amounts of insulin in response to changes of the plasma glucose level, may be impaired in

their ability to counteract the effects of stress hormones. As a result, IDDM patients may be particularly prone to the development of marked or prolonged stress hyperglycemia.

Evidence supporting this hypothesis has come from studies manipulating stress hormones (i.e., assessing the infusion of stress hormones into patients). For example, Shamoon, Hendler, and Sherwin (1980) compared the hyperglycemic effect of epinephrine infusions in normal subjects and in subjects with IDDM. They provided data suggesting that IDDM patients exhibit increased sensitivity to infused cortisol and catecholamines when compared to normal individuals, so that the hyperglycemic response to those hormones is more marked. Gerich, Lorenzi, Tsalikian and Karem (1976) have shown that epinephrine release induces hyperglycemia in humans, and Baker, Minuchin, Milman, Leibman, and Todd (1975) have shown that children with diabetes have a more rapid increase in blood ketones concentration following epinephrine infusion than do nondiabetic children. Baker, Kay, and Hague (1967) assert that in labile adolescent patients, emotional stress leads to mobilization of free fatty acids and ketoacidosis mediated by counter-insulin stress hormones, especially by the catecholamines and cortisol. Hamburg and Inoff (1982) showed that small increments of plasma epinephrine produced a marked reduction in glucose tolerance in otherwise healthy persons by interfering with insulin action.

There is research evidence implicating stress and its hormonal consequences in precipitating or exacerbating hyperglycemia in diabetes. For example, Christensen (1983) reported high levels of plasma catecholemines in poorly controlled diabetic patients when compared to patients with good control. Schade and Eaton (1980, 1983) show in their data that metabolic decompensation may be precipitated by stress-induced counter-regulatory hormones even in the presence of insulin.

The above studies demonstrate the importance of conterregulatory hormone influence on metabolic control. However, studies actually manipulating stress (i.e., stress-induction procedures) have led to mixed results with blood glucose sometimes showing an increase (Barglow, Hatcher, & Edidin, 1984), decrease (e.g., Hinkle & Wolf, 1951, 1952), or no significant change (e.g., Kemmer, Bisping, & Steingruber, 1986). These discrepant results may be due to methodological problems and will be discussed in detail later.

Regimen Adherence

Most studies have emphasized psychophysiologic explanations of the impact of stress on metabolic control. Stress, however, can also affect adherence to the diabetic regimen and thus alter diabetic control through disruption of dietary compliance, activity level, insulin use, or the

self-monitoring of glucose levels. These changes in behavior may often explain the presence of hyperglycemia. In a study by Kirkley (1982), the impact of stress on adherence was manifest in self-reports of 57 diabetics regarding antecedents of eating too much or eating the wrong foods. They attributed 19% of such violations to negative emotions and another 7% to conflict. Cohen, Vance, Runyan, and Hurwitz (1960) reviewed 72 cases of ketoacidosis and found that the most common precipitating factor (27%) was the omission of insulin. In half of these cases insulin omission was attributed to psychological stress.

Most studies assessing effects of stress on diabetic control fail to separate adherence to treatment from hormonal mediation as the major agent relating stress and diabetic control. Further, their designs are also marred by the use of only a small number of subjects and a paucity of metabolic and psychologic quantification.

In summary, if stress does affect diabetes control it exerts its action by altering either or both the "internal milieu" (stress hormones), or the "external milieu" (patient's compliance). Both means of action may be operating simultaneously since stress reduction affecting levels of neuroendocrine substances could also increase or decrease adherence to medical regimen. Stress reduction could facilitate diabetic control if high levels of stress could be proven to change compliance behavior or to produce

large, rapid, or prolonged changes in carbohydrate and fat metabolism.

Methodology for Studying How Stress Affects Physiology and Metabolic Control

Two approaches have been taken by investigators studying psychologic stressors. One approach is correlational and assesses the relationship between naturally occurring, psychologically stressful events and blood sugar control. The second is experimental and assesses the effect of acute laboratory stressors on metabolic control in diabetic or nondiabetic individuals.

Correlational

The more common approach is correlational. In these studies, life stress is defined as the occurrence of events which require significant change in life patterns. Such events include losing a close friend, moving to a new home, parents' divorce, etc. It is commonly assumed that high levels of change in a short period of time may have a cumulative impact on the individual and may contribute to problems of health and adjustment.

Evidence supportive of a relationship between undesirable life events and changes in a patient's metabolic condition can be found in investigations of adults with the

disease. For example, Grant, Kyle, Teichman, and Mendels (1974) using a modification of Holmes and Rahe's Schedule of Recent Life Events inventory observed a positive correlation (+.40 or greater) between undesirable life events and the patients' diabetic condition in a sample of 37 patients with diabetes. In this study negative events accounted for most of the variance.

Bradley (1979) examined individual measures of physical state in relation to retrospective measures of life events experienced over a 12 month period. She found that the number of stressful life events was associated with diabetes control in adults. More specifically, increases in the incidence of glycosuria, changes in prescriptions and frequency of clinic attendance were associated with increases in the reported occurrence of life events. However, the experience of life events was not reflected in blood glucose measures.

Another example of this approach is provided by Bedell, Giordani, Amour, Tavormina, and Boll (1977) who studied the relationship between life stress and day-to-day health using a sample of 45 chronically ill children (40% with diabetes) attending a 3-week residential summer camp. These investigators found life stress to be correlated with the frequency of acute symptoms by youngsters during the camp session, suggesting that life stress may be related to the day-to-day health status of chronically ill children.

Campers who had a high incidence of pre-camp life stress had significantly more illness episodes during their camp stay than campers with low life stress.

Chase and Jackson (1981) in a study of children with diabetes demonstrated that high stress scores on the Coddington Life Events Record (Coddington, 1972), which provided a general measure of life change during the preceding 3 months, were correlated with decreased short and long term glucose control as measured by triglyceride concentrations, percent Hemoglobin A1, cholesterol values,, and serum glucose concentrations. However, this relationship between increased stress and decreased metabolic control could only be found for 15-18 year old patients.

Studying younger patients, Brand, Johnson, and Johnson (1986) also found a relationship between undesirable life experiences prior to a summer camp and metabolic control (only significantly related with urine ketones) during the camp stay, but only for 10-12 year old male children, with an internal locus of control.

While there appears to be some evidence that negative life stress is associated with poorer metabolic control, findings are not always consistent from study to study and the strength of the relationship between stress and control is usually weak. Life event checklists have inherent problems. The major shortcoming is that they tap major life

events that occur relatively infrequently in the general population. Additionally, individual patients may experience various life events differently and a particular patient's stressful experiences may be missing from the checklist. Major life events are only one type of stress and are probably not representative of the daily hassles one experiences in living. Therefore, day-to-day stress may be a more important influence on metabolic control than occasional, albeit undesirable, "life events."

A measure that taps day-to-day hassles and frustrations has recently been developed (Kanner, Coyne, Schaefer, & Lazarus, 1981). Scores on the Hassles Scale have been related to the development of psychological and physical symptoms and also account for most of the variance attributable to major life events (DeLongis, Coyne, Dakof, Folkman, & Lazaraus, 1982). Little research has been conducted on the relationship between everyday stress and metabolic control (compared to major life events), even though recent evidence suggests that minor life events scales may have more utility than major life events scales in predicting health outcome (Kanner et al., 1981).

Cox et al. (1984) assessed the relationship between daily hassles or irritations and diabetic control in a sample of 59 adult IDDM patients. A significant positive correlation ($r = .25$, $p<.05$) was found between daily hassles

and hemoglobin A1 levels. However, once again, the strength of the relationship was relatively weak.

Another problem with correlation research is that most field studies have not taken subjects' insulin, diet, and exercise regimens into account. In an unusual study, Hanson and Pichert (1986) assessed whether stresses perceived on a day-to-day basis influenced blood glucose levels in IDDM patients, statistically controlling for insulin, diet, and exercise. When stress was broken down into positive and negative components, negative cumulative stress was significantly related to blood glucose levels in the children. These findings suggest that minor stressors can influence health outcome. However, positive and negative stress need to be assessed independently, and the influence of other variables (e.g., food, exercise, insulin) needs to be controlled.

Although it is typically assumed that stress causes poor metabolic control, it is possible that poor metabolic control could be causing the stress. Mazze et al. (1984), for example, found that changes in glycemic control were consistently related to changes in reported anxiety, depression, and quality of life. It is certainly possible that health status may contribute to patients with diabetes psychological stress as opposed to stress affecting the patient's health status. The bidirectionality of the

stress/health status relationships makes the interpretation of correlational data most difficult.

Experimental

Studies that have directly manipulated stress in diabetic patients have used stressors including stress induction interviews (Baker et al., 1975; Hinkle, Conger, & Wolf, 1950; Hinkle & Wolf, 1952; Minuchin, Rosman, & Baker, 1978), hypnosis (Vandenbergh, Sussman, & Titus, 1966), and shock (Vandenbergh, Sussman, & Vaughn, 1967). For example, Hinkle and Wolf (1952) studied diabetic subjects (IDDM and NIDDM) and nondiabetic subjects individually during baseline, stress (interview), and post-stress phases. This format was used in the fasting state with diabetic subjects receiving no insulin before the stress. During the stress phase blood ketones and urinary output increased and blood glucose levels showed a decrease for most but not all subjects. Similar results in diabetic subjects were reported by Vandenbergh and his colleagues (Vandenbergh, Sussman, & Titus, 1966; Vandenbergh, Sussman, & Vaughn, 1967). Vandenbergh, Sussman, and Vaughn (1967) found that a task involving an unpredictable shock produced a significant decrease in glucose concentration and nonsignificant increases in free fatty acid (FFA) and urine volume in six diabetic patients and an inconsistent response pattern in nondiabetic controls. Hypnotically induced emotional stress

also caused a decrease in blood glucose levels in diabetic patients and nonsignificant increases in FFA and urine volume (Vandenbergh, Sussman, & Titus, 1966).

In contrast, Baker et al. (1975) reported an increase in glucose during a stress interview. Two preadolescent girls with diabetes were studied, both of whom had a history of multiple hospitalizations for severe diabetic ketoacidosis. A specific stress interview with one child caused free fatty acid concentrations associated with significant increases in plasma corticosteroids and growth hormone concentrations as well as increased urinary excretion of epinephrine. Beta-adrenergic blockade prior to a repeat stress interview blocked the metabolic changes without interfering with the hormonal response to stress.

The few studies that have investigated the question systematically have shown that increases in blood ketones, FFA and urine volumes were the changes most consistently associated with stress. Interestingly, these studies show variability or even decreases in blood glucose in response to stress (Vanderbergh, Sussman, & Titus, 1966; Minuchin et al., 1978; Lustman, Carney, & Amado, 1981). Urine glucose measures appeared to be least sensitive to the stress manipulations (Hinkle et al., 1950; Vandenbergh, Sussman, & Vaughan, 1967). The results of these initial investigations demonstrated that although psychologic stressors may elevate plasma free fatty acid levels, urine ketone levels and urine

volume, the effect on blood glucose levels is less consistent. While stress appears to be a destabilizing stimulus, these controlled studies did not support the conclusion that acute stress is a hyperglycemia-inducing event.

While these early studies made an important contribution, they suffer from serious methodological flaws. Most exerted relatively poor control over conditions, few made efforts to counterbalance the designs to control for order effects, and most lacked consistent dependent measurement. Much of the work is case-study oriented (although some studies used nondiabetic comparison subjects), lacks statistical tests of significance, used highly heterogeneous subjects (e.g., mixed IDDM and NIDDM), and did not carefully measure the participants experience of stress by self-report and by psychophysiological indices. The stress manipulation used may have been experienced as more or less stressful by different subjects, introducing substantial variability into what appeared to be a well-controlled experiment. Another methodological concern is the lack of control for effects of insulin use and carbohydrate ingestion before the studies.

For many years following this early work, few studies were conducted assessing the acute relationship between psychological stress and blood glucose level in diabetes, perhaps due to methodological difficulties unique to this

research area. However, in recent years there have been several more sophisticated, systematic studies conducted which analyze the effects of stress on IDDM subjects.

Kemmer et al. (1986) assessed the effect of acute psychological stress (mental arithmetic and public speaking) on metabolic control and glucoregulatory hormones in normal subjects and normoglycemic and hyperglycemic IDDM patients. Each subject was studied on three days for 140 minutes, approximately 1.5 hours after a standard breakfast. The normoglycemic IDDM group took their usual insulin doses the evening before and on the morning of the study. The hyperglycemic group injected only regular insulin the evening before the study and withheld their usual insulin injection on the morning of the study to induce an acute state of poor metabolic control. On the first day the subjects received no stress. On each of the other two days after a 10 minute baseline, the subjects experienced a stress period of either 15 minutes (public speaking) or 45 minutes (mental arithmetic) and a recovery period of 105 or 75 minutes. Blood glucose was analyzed every 5 minutes for the first 15 minutes (during the stress period) and every 15 minutes for the next 3 measurements (until time 60) then every 30 minutes for the rest of the study. These psychological stimuli produced marked cardiovascular responses and moderate elevations in plasma concentrations of epinephrine, norepinephrine, and cortisol. However,

concentrations of blood glucose, plasma ketone bodies, and free fatty acids did not increase in any of the groups compared to the no stress day.

Similar results were found by Delamater et al. (1988) in a study assessing the physiologic effects of acute psychological stress in adolescents with IDDM. Subjects, divided into good, fair and poor metabolic control groups, were studied in the morning prior to insulin and breakfast. Physiologic responses were determined before and after three 10-minute stressors (cognitive quiz, family interaction-disagree, and family interaction-neutral) administered over 80 minutes. Although subjective and cardiovascular responses to stress occurred, significant metabolic and hormonal changes as a result of the stress were not observed for any of the groups.

In a similar study, Gilbert, Johnson, Silverstein, and Malone (1989) reported consistent findings studying two IDDM adolescents groups (good versus poor metabolic control) and nondiabetic controls. Patients took their insulin and ate breakfast the morning of the experiment. Metabolic indices were measured only at the beginning and the end of the experiment. Despite increases in anxiety and arousal to the three stressors (venipuncture and two public speaking tasks) separated by brief rest periods, there was no evidence that the stressors produced derangements in metabolic control in any of the groups studied.

Edwards and Yates (1985) measured blood glucose levels and subjective estimates of stress levels in 45 minute baseline sessions on three successive days in IDDM and nondiabetic groups. Each session began at 2 p.m., 2 hours after the subject's last meal and 8 hours after the last insulin injection. On two subsequent days half of each group performed a high demand and half a low demand task, blood glucose levels and subjective stress levels being assessed before, during and after the stress period. Stress did not appear to induce significant changes in blood glucose level in any of the groups even though subjective stress level measures indicated that the task was stressful. Thus, recent studies of the effects of stress on metabolic control in IDDM do not reveal altered blood glucose levels associated with psychological stress.

There has been no recent work which provides empirical data utilizing laboratory psychological stress-induction studies in human NIDDM subjects. Researchers have indirectly studied the effects of stress on diabetes control by investigating the effects of relaxation techniques. Since relaxation techniques appear to decrease sympathetic nervous system activity (Degood & Redgate, 1982), relaxation therapy may serve to moderate some of the negative effects of the stress response on metabolic control. In a well controlled study, Surwit and Feinglos (1983a,b) studied the acute effects of relaxation training on glucose tolerance in

NIDDM patients. Glucose tolerance improved significantly in patients who received progressive muscle relaxation training as compared to a control group. Subjects receiving relaxation showed a decrease in plasma cortisol, whereas control subjects showed an increase over the same time period. Lammers, Naliboff, and Straatmeyer (1984) showed that progressive muscle relaxation significantly lowered blood glucose levels in two of four NIDDM subjects. The researchers noted that this positive response may be especially likely to occur in those patients with initially elevated glucose levels and less stable metabolic control.

In contrast, relaxation interventions with IDDM subjects have provided mixed results (Fowler, Budzynski, & Vandenbergh, 1976; Landis, Janovic, & Landis, 1985; Feinglos, Hastedt, & Surwit, 1987). Feinglos et al. investigated the effect of treatment with biofeedback-associated progressive muscle relaxation on poorly controlled IDDM subjects compared with equivalent untreated patients. In contrast to previous studies of NIDDM subjects, relaxation had no effect on glucose tolerance and several indices of metabolic control. These data are consistent with Landis et al. (1985), who found a reduction in the daily range of blood glucose levels, but no significant change in average glucose levels, glycohemoglobin, or insulin requirements in stable IDDM patients after 15 weekly sessions of relaxation training and

3 monthly follow-ups. These negative findings contradict earlier case reports that suggest that relaxation training lowered insulin requirements and reduced the frequency of ketoacidosis in IDDM patients (Fowler et al., 1976; Seeburg & DeBoer, 1980).

Based on the results of animal model studies and chemical infusion studies indicating altered sympathetic nervous system (SNS) activity in NIDDM, Surwit and Feinglos (1988) proposed a model describing the impact of stress in NIDDM. They suggest that increased alpha-adrenergic sensitivity in the endocrine pancreas and other tissues in NIDDM leads to an exaggerated suppression of insulin secretion and glucose utilization, leading to an exaggeration of SNS effects upon glucose metabolism. Their model does not require the presence of unusual psychologic stress for metabolic dysregulation to occur since the metabolic effects of even normal SNS activity appear to be exaggerated.

Although the Surwit and Feinglos (1988) model is of interest, it is clear that, there is a great paucity of sophisticated studies assessing the direct effects of stress on diabetes control in NIDDM patients.

The failure to find a direct link between stress and hyperglycemia might be attributable to methodological defects as well as other unmeasured mediating factors. For example, some investigators have emphasized the need to

consider the patient's coping response (Brand et al., 1986; Delamater, Kurtz, Bubb, White, & Santiago (1987) and Type A or B behavior patterns (Cox et al., 1984; Stabler, Morris, Litton, Feinglos, & Surwit, 1986) as a possible moderating influence on stress/metabolic control relationships. Additional variables of this type that have been mentioned in the literature include whether the stress is impersonal or has personal relevance and importance to the patient, the difference between anticipation of stress and the stress itself, and whether the stress is predictable or unpredictable (or controllable or uncontrollable). This area of research reveals the importance of standardizing the stressor and utilizing manipulation checks when studying the effects of stress on metabolic control.

Autonomic activation is no longer thought of as a relatively fixed pattern independent of varying environmental demands and intended goals as originally inferred by Selye's "nonspecific stress response." Investigators (e.g., Mason, 1975) now suggest that the endocrine system, as well as the autonomic system exhibits "situational stereotypy"--with differing events evoking distinctive patterns of integrated hormonal response. For example, Lunberg and Frankenhaeuser (1980) found two distinct responses to stress by varying experimental conditions and performing a factor analysis. They discovered that pituitary-adrenal activation (cortisol

excretion) was associated with negative feelings of distress, and sympathetic-adrenal activation (epinephrine excretion) with feelings of alertness and action proneness. These data are consistent with other studies (Henry & Stephens, 1977; Levine, Weinberg, & Brett, 1979; Ursin, Baade, & Levine, 1978; Cox et al., 1984) which conclude that different endocrine systems are stimulated by different types and severity of stressors.

There is also evidence to suggest that individuals may respond idiosyncratically to stress--termed response specificity. For example, Elwood, Ferguson, and Thakar (1986) found both increases and decreases in catecholamine levels in response to a stressor situation (cognitive tasks), with an increase representing an adaptive response and a decrease representing a less adaptive response.

This area of research shows that it may be important, when designing a study involving stress effects, to have each subject serve as their own control (in addition to having control groups). The data from this type of design need to be analyzed between groups and within subjects to help assess idiosyncratic responses to stress.

Therefore, it appears that it is not just the stimuli or physical environment per se that determines the physiological response, but the individual's evaluation of these stimuli. This point indicates the importance of

subjective appraisal of the stress situation (or perceived stress).

It should be clear from the foregoing discussion of the existing literature in this research area that the investigations conducted to date present contradictory findings in their studies of the relationship between stress and metabolic control. The two potential mechanisms by which stress could affect metabolic control (physiological effects of hormones versus regimen adherence) have not been clearly distinguished from each other by existing studies.

The discussion of the methodological problems and potentially influential mediating variables discussed above emphasizes the importance of a well designed study utilizing a standardized stressor, subjective self-report data in addition to physiological indices for measuring stress and most importantly, using each subject as their own control in a repeated measures design.

Such a study conducted by Wing, Epstein, Blair, and Norwalk (1985) provides a starting point for sorting out some of the discrepancies in the data. Wing et al. (1985) assessed the effect of a standardized psychological stressor on blood glucose levels in nondiabetic subjects. All subjects participated in two sessions (stress/nonstress) presented in counterbalanced order. After a 20-minute baseline, fasting subjects consumed a carbohydrate load. On nonstress days subjects relaxed after the drink; on stress

days, subjects participated in competitive tasks for 30 minutes after the drink. Blood glucose responses were measured at 0, 30, 60, 90, and 120 minutes after the load. Results show that stress impaired nondiabetic subjects' ability to handle a carbohydrate load. Stress did not raise or lower blood glucose levels but rather caused a temporal shift (30 minutes) in the glucose curve. These results demonstrate that direction of blood glucose may hinge on when blood samples are obtained and when the stress is administered with respect to the last meal.

Most stress-induction studies measure blood glucose before, and at one time after, the stressor. In the Wing study, if only one blood sample had been obtained at 30 minutes, stress would have appeared to lower blood glucose. If the sample had been taken at 60 minutes, stress would have appeared to raise blood glucose. This important study may point out a prime explanation for why previous data assessing the effect of psychological stress on glycemic control in diabetes are so variable. The next obvious step is to replicate this study using diabetic subjects. As emphasized above, IDDM and NIDDM patients should be evaluated separately.

In conclusion, many of the existing studies on the effects of stress on metabolic control have methodological defects such as poorly controlled conditions, few efforts to counterbalance the designs to control for order effects,

inappropriate subject groups, lack of consistent dependent measurement, and failure to measure the participants' experience of stress by self-report and psychophysiological indices. In addition to methodological defects, it appears that stress effects may be modified or mediated by a number of different factors including the type of stressor employed, the availability of endogenous insulin, presence of Type A/B behavior pattern and coping mechanisms. There is also evidence to suggest that individuals respond idiosyncratically to stress. Although the recent work by Wing et al. (1985) overcomes many of the defects characteristic of earlier work, the present study goes beyond the Wing et al. (1985) research by taking more frequent blood samples and by using IDDM and NIDDM subjects.

The present study attempted to minimize the effects of differences in diet, exercise, and insulin dose, and utilized appropriate subject groups, a standardized stressor, a repeated measures design with consistent, frequent measurement of the dependent variables using each subject as their own control (in counterbalanced order), as well as self-report and psychophysiological measures.

This study was designed to test the following hypotheses:

1. Because the present study is a modified replication of the Wing et al. (1985) study, it is hypothesized that the response of the nondiabetic group will

be reproduced: stress will not raise or lower blood glucose levels but will cause a temporal shift in the glucose curve.

2. As described in the introduction, the pancreatic islets of IDDM patients are unable to respond normally to changes in plasma glucose level. Therefore, it may be difficult for them to counteract the effects of stress hormones. As a result, IDDM patients may be particularly prone to the development of stress hyperglycemia (as compared to nondiabetic controls).

3. As has recently been hypothesized (Surwit & Feinglos, 1988), NIDDM may be related to abnormalities in the sympathetic nervous system. In particular, enhanced sensitivity of the alpha2-receptors in the pancreas and elsewhere can lead to exaggeration of sympathetic nervous system effects and the impairment of both insulin secretion and glucose utilization. This metabolic malfunctioning may occur even in the absence of unusual psychological stress. Because psychological stress stimulates sympathetic nervous system activity, NIDDM patients may be extremely sensitive to the effects of psychological stress.

It is hypothesized that NIDDM patients will exhibit greater stress hyperglycemia than normal controls.

4. Patients with IDDM and NIDDM may have different responsiveness to stress since stress reduction studies evidence disparate consequences of relaxation therapy on these two patient populations (Feinglos et al., 1987). The

results of the Feinglos et al. series of studies showed that NIDDM patients responded positively to relaxation training whereas IDDM patients do not, suggesting that the direct physiologic effects of stress may possibly be more important in patients with NIDDM. Therefore, it is hypothesized that NIDDM patients may show greater stress hyperglycemia than IDDM.

CHAPTER 2
METHODS

The present investigation differed from past attempts to study the effects of stress in persons with diabetes in a number of important respects. This study used appropriate subject groups (e.g., separated IDDM and NIDDM groups); tightly controlled conditions that minimized the effects of differences in diet, exercise, and insulin dose; used a standardized stressor; used each subject as his/her own control (in counterbalanced order); used self-report and psychophysiological measures; and used consistent, frequent measurement of relevant dependent measures. The study assessed whether the standardized stressor was "perceived" as stressful subjectively (via self-report measures), psychophysiologically (via heart rate), and physiologically (via plasma cortisol) and whether the stressor had an effect on glycemic control (via blood glucose) of IDDM, NIDDM, and nondiabetic controls.

Participants

Participants consisted of IDDM, NIDDM, and nondiabetic control subjects. These subjects were studied in the Clinical Research Center (CRC) at the J. Hillis Miller

Health Center, University of Florida, Gainesville. Subjects were recruited from the following: lists of diabetic patients provided by the Diabetes Clinic at the J. Hillis Miller Health Center and local physicians, advertisements placed on bulletin boards or in newspapers, and word of mouth. The age range was from 18 to 65 years.

Criteria for inclusion in the diabetic groups included diagnosed IDDM for at least three years or NIDDM of one year. Noninsulin-dependent diabetes mellitus subjects with a current or past history of exogenous insulin use were excluded. All subjects were free from major medical problems (e.g., no diagnosed cardiovascular or neurological abnormalities), and except for insulin and hypoglycemic oral agents, were not taking any medications which would affect heart rate or carbohydrate metabolism. They were not taking antihypertensive medications (fludrocortisone or beta-adrenergic antagonists, or diuretics) and they were not on salt restricted diets. Subjects with autonomic diabetic neuropathy were screened out.

Nondiabetic subjects were healthy, with no immediate family history of diabetes and normal fasting blood glucose and Hemoglobin A1c (HbA1c) levels. The HbA1c is a measure of the amount of glucose adhering to hemoglobin in the blood and reflects average blood glucose over 2 - 4 months (Tarnow & Silverman, 1981-1982). Diabetic and nondiabetic subjects

were matched on sex, age, and Body Mass Index (BMI) [BMI = weight(kg)/height^2(m)][1] (Garrow, 1981).

General Procedure

Screening

Subject screening was conducted via a generalized screening questionnaire (Appendix A) designed to exclude subjects who were clearly unacceptable for the study. Acceptable subjects were scheduled for an appointment on the CRC for further screening. During this appointment, the subjects were formally tested for diabetic autonomic neuropathy via an assessment of the R-R interval: a test measuring immediate heart rate increase after rising from a supine position (Ewing, Campbell, Murray, Neilson, & Clarke, 1978) (refer to Appendix B for procedure). If the patients' test ratio (length of the R-R interval at beat 30 following standing divided by the length of the R-R interval at beat 15) was less than 1.0, they were excluded from the study. Otherwise the patient was asked to complete the Social Readjustment Rating Scale (Holmes & Rahe, 1967) (Appendix C) for life events occurring during the past month--significant items were clarified by the subject. If the subject was

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[1]Body Mass Index is a way of incorporating height and weight into one measurement in order to more easily match subjects and assess the degree of overweight. A BMI of 27 is considered 20% overweight.

experiencing major life stress or an unusual life event, scheduling was postponed or the subject was excluded. Procedures of the study were explained in detail to acceptable participants both verbally and in writing and consent was obtained in writing.

Study Protocol

Subjects were scheduled to attend two sessions, separated by 1-7 days. These two sessions included a stress and a nonstress or control condition, presented in random order. Subjects were instructed to fast (including coffee and cigarettes) from midnight and arrive at the laboratory at approximately 8:15 a.m.

Height and weight were recorded and a Sears Digital Electronic Heart Rate Monitor was attached to the subjects' ear for continuous monitoring of heart rate (recorded every 60 seconds from a digital display readout). A heparin lock was placed in the nondominant arm for pain-free monitoring of blood glucose throughout the experiment. At this time, a blood sample was taken, centrifuged, and analyzed for plasma glucose concentration (via a Beckman Analyzer in the CRC--enzyme hexokinase technique), Hemoglobin A1c (via a column chromatography method--Bio-Rad's by Column Test), and cortisol (by Dr. Neil Rowland via a commercial radioimmunoassay kit by Diagnostic Products). All subsequent blood draws were managed and analyzed in this

manner (except the HbA1c analysis which was performed once per diabetic subject).

Insulin-dependent diabetes mellitus subjects were instructed to take their insulin, and NIDDM subjects on oral hypoglycemic agents took their medication. After ten minutes the baseline period began. Nondiabetics and diet-only NIDDM subjects began the session with the baseline period.

Each session began with a 20-minute baseline period, during which the subject sat quietly, reading or watching T.V. At the end of the baseline period, a blood glucose sample was obtained. Subjects then completed two short self-report inventories: the A-State portion of the State/Trait Anxiety Inventory (STAI) (Speilberger, Gorsuch, & Lushene, 1970) and a paper and pencil version of the "Self-Assessment Manikin" (SAM) (Hodes, Cook, & Lang, 1985) (Appendix D). The subject then consumed an 8-oz can of Sustacal (Mead Johnson Nutritionals) within 1-2 minutes. This mixed meal beverage contains 240 kcal (1 Calorie/ml), 33.1 grams (55%) of carbohydrate, 14.5 grams (24%) of protein, and 5.5 grams (21%) of fat per 8-oz can. The time at which the subject finished the last sip of the beverage was recorded as t = 0. Blood samples were drawn (approximately 4 ml) for glucose and cortisol analysis taken via the heparin lock at t = 10, 20, 30, 45, 60, 75, 90, 105, and 120 minutes. At t = 30 subjects completed the same

self-report inventories. Exactly the same schedule of blood samples and self-report measures were used on stress and nonstress (control) days. Stress and control sessions were performed at the same time of the day in order to avoid errors introduced by duration of fasting.

On control days, subjects sat quietly and watched a videotaped documentary during the 120 minute period following the Sustacal load.On stress days, subjects participated in a psychologic stressor for the 30 minutes period immediately following the drink (t = 0-30) and then watched a similar videotape for the remaining 90 minutes (t = 30-120).

Standardized Psychological Stress Manipulation Task

The stressor involved a variety of tasks (3) presented via an (IBM compatible) laptop computer (NEC Multispeed). Subjects were told that they have the opportunity to win more money (in addition to their $20.00 subject participation money) by partaking in these tasks. The tasks changed every 10 minutes and included mental arithmetic, falling numbers and matching. For each correct answer the subject won 20 cents, for each incorrect answer they lost 20 cents. Subjects were informed that although it has not occurred with other subjects so far, there is a chance that they could actually lose money.

The computer program (developed by Craig S. Lipman and the candidate) is designed (in Clipper--compiled dBase language) so that the level of difficulty of the task adjusts to the skill level of the participant forcing the participant to achieve and maintain a 40 percent accuracy --so that it will not be too easy or too hard for them; the better they do the harder it gets, the worse they do the easier it gets. The program accomplishes this by tracking the participants performance. The logic for adjusting the difficulty is as follows: The difficulty level will increase if all of the following are true: 1) The total percent correct is greater than 40.5 percent; 2) at least two of the last four attempts were correct, and 3) the difficulty level was not previously adjusted within the last four attempts.

The level of difficulty will decrease if the following are true: 1) The total percent correct is less than 39.5; 2) at least two of the last four attempts were incorrect, and 3) the difficulty level was not previously adjusted within the last four attempts.

Additionally, the program was designed so that all subjects lost the same amount of money and they were aware of how much as the tasks continued because it was displayed on the computer screen. Subjects were debriefed immediately after completing the post self-report questionnaires and received the full $20.00 at the end of the study.

Self-Report Measures

Subjects completed the State portion of the State-Trait Anxiety Inventory ("Self-Evaluation Questionnaire"), and the SAM (Self-Assessment Manikin) at the beginning of each session and at t = 30 (just after the psychologic stressor--on stress days).

The State portion of the STAI consists of 20 statements that ask the individual to indicate how they feel at a particular moment in time. The Scale is designed to be self-administering--the subject merely has to indicate one of four possible responses for each statement: not at all, somewhat, moderately so, or very much so. The manual specifically states that "researchers can use the A-State scale to determine the actual levels of A-State intensity induced by stressful experimental procedures." The manual notes that it has been shown that scores on the A-State scale increase in response to various kinds of stress and decrease as a result of relaxation training (Speilberger et al., 1970).

SAM Administration. The SAM is an instrument designed to obtain ratings from subjects on three independent affective dimensions: pleasure (valance), arousal, and dominance (control). This instrument presents analogue representations for each dimension (e.g., for pleasure, a human-like figure with a series of facial expressions ranging from smiling to frowning). The SAM is available as

a computer program or a paper-and-pencil measure, which is the form used in this study. Subjects were instructed to place an X on one of the five pictures or in between them, allowing for a 9-point rating scale.

The following instructions, adapted from Hodes, Cook, and Lang (1985) were verbally communicated to the subject:

> In addition to your physiological responses, we are interested in your emotional feelings. In order for us to obtain information about emotions in a standard way, you will use a "self-assessment manikin" or SAM. SAM can be used to represent the way you feel. You will use SAM to report three separate dimensions of feeling: happy-unhappy, excited-calm, in control-controlled. These feelings are experienced along a scale from maximum to minimum. At one extreme of the happy-unhappy scale your are: happy, pleased, satisfied, contented, hopeful. These words describe a similar feeling. When you feel completely contented, SAM should look like this. (Point to SAM with maximum pleasure). Now let's look at the opposite feeling from pleasure--at the other end of the scale. This is the way SAM should look when you feel completely: unhappy, annoyed, unsatisfied, melancholic, despairing, bored. (Point to SAM with minimum pleasure). This is what SAM will look like when you feel completely neutral, neither happy nor really unhappy. (Point to SAM with neutral pleasure). By picking pictures of SAM between the minimum and neutral and maximum you can make SAM show just how you feel, not just completely satisfied or completely unsatisfied, but in between. (pp. 558-560).

Instructions were explained in a similar way for the "excited-calm" dimension and the "in control-controlled" dimension. Time was taken to make sure the subject understood each dimension and examples were used to assess this.

Physiological Measures

Heart Rate

One sympathetic response to psychological stress is an increase in heart rate.

Heart rate data was collected using the Sears Digital Electronic Heart Rate Monitor, accurate to approximately 2 BPM, at 60 second intervals throughout each session.

Blood Glucose

The major dependent measure in this study was bloody glucose. After the baseline blood sample, additional samples were collected, centrifuged, and analyzed (via the Beckman Analyzer, accurate to within 2-4 mg/dl) at 10, 20, 30, 45, 60, 75, 90, 105, and 120 minutes after the Sustacal load.

Cortisol

Plasma cortisol levels were measured to assess they role of stress in cortisol release and its relationship to glucose fluctuation. Plasma (0.2 - 0.4 ml) from each blood draw was transferred into a small plastic vial, labeled, frozen and delivered to Dr. Neil Rowland's Psychobiology Lab for analysis via a commercial radioimmunoassay kit by Diagnostic Products.

Data Analysis

All statistical analyses were conducted using the statistical package--PC SAS on a IBM compatible PC. The main analysis used was a repeated measures analysis of variance, with Group (IDDM/NIDDM/Nondiabetics) as a between subject factor and Condition (Stress/Control) and Time (each measurement period) as repeated measures. All analyses were 2-tailed with a p value of .05.

CHAPTER 3
RESULTS

Description of Sample

Thirty-four subjects participated in the study including 9 IDDM, 9 NIDDM and 16 nondiabetic control subjects. Diabetic subjects were matched with nondiabetic control subjects according to age, sex, and Body Mass Index (BMI). All subjects were Caucasian.

Six subjects from the original selected sample size of 10 IDDM, 10 NIDDM, and 20 nondiabetic controls had to be dropped from the study for a variety of reasons. One IDDM subject fainted after the second blood draw (diagnosed as a vago-vagal response) on day two of the study and was subsequently dismissed after receiving medical attention and fully recovering from the incident. One NIDDM subject was dropped due to the lack of any "stress effect" during the stressor. He essentially "gave up" after realizing during the first few minutes of the stressor that he "could not win." Self-report, heart rate, blood glucose data, and behavioral observations all confirmed the absence of a stress effect. Four nondiabetic control subjects were dropped from the data set. All four were set up to be matched with NIDDM subjects and tended to be older and

heavier. Two of the subjects were untestable due to great difficulty locating a suitable vein for adequate blood draws. Acceptable veins were located for the other two subjects, but proved to be deficient for properly timed blood draws for the duration of the study. Therefore, due to clotting, difficulty drawing blood and a need for reinsertion of the heplock, missing data, and off time blood draws ensued. A total of 16 complete matches remained, with one extra nondiabetic control subject for the IDDM group and a deficiency of three nondiabetics for the NIDDM group.

Insulin-Dependent Diabetic Subjects (IDDM)

The IDDM group included 5 male and 4 female subjects with a mean age of 26.2 years (range: 20 - 37) and an average BMI of 22.3. The mean number of years for duration of illness was 15.2 years. As indicated by their HbA1c levels, most subjects were in adequate control (mean = 7.7, indicating mild hyperglycemia) during the few months before their participation in the study. In our laboratory, normal HbA1c levels range from 3.5 to 6.1. Mild hyperglycemia is evidenced by a range from 6.2 to 8.3; moderate: 8.4 - 11.2; and severe: 11.3 and up. All subjects were undergoing treatment with conventional insulin therapy. Refer to Table 1 for individual subject data including exact insulin types and dosages.

Table 1. Individual Subject Information

IDDM								
							Insulin	
ID	Sex	Age	BMI	HbA1C	R-R	Dur DM	AM	PM
9	F	21	21.9	6.1	1.09	11.5	10 R 24 NPH	5 R 12 NPH
12	M	26	23.5	6.5	1.06	24	8 R 17 NPH	10 R 16 NPH
14	M	20	21.7	7.5	1.25	17	10 R 24 NPH	6 R 8 NPH
15	F	37	18.7	7.3	1.14	22	20 R	20 R 2 NPH
16	F	24	18.8	7.6	1.06	12	10 R 20 NPH	6 R 6 NPH
18	M	20	25.1	13.1	1.1	8	10 R 30 NPH	10 R 30 NPH
19	M	34	25.0		1.2	6	20 NPH	5 NPH
21	M	20	24.3		1.12	5	18 R 30 L	18 R 12 L
40	F	34	22.7	5.9	1.18	31	32 L	16 L
Mean		26.2	22.3	7.7	1.13	15.2		

Table 1. Continued

							NIDDM	
							Insulin	
ID	Sex	Age	BMI	HbA1C	R-R	Dur DM	AM	PM
13	F	32	31		1.26	7	5 Micronase	
17	M	44	28	8.5	1.11	22	10 Micronase	
23	M	37	35	6.3	1.06	1	Diet Only	
28	F	45	41	5.1	1.25	3	Diet Only	
30	F	64	29	5.5	1.15		2.5 Micronase	
31	F	63	25	7.4	1.05	2.5	2.5 Diabeta	
32	M	54	22	5.5	1.1	2	Diet Only	
35	F	64	23	8.1	1.09	1	5 Diabeta	
42	F	64	28	5.9		4		2.5 Glucont
Mean		51.9	29.5	6.5		5.3		

Table 1. Continued

Nondiabetic (ND1)			
ID	Sex	Age	BMI
1	M	25	23.3
3	M	29	20.5
4	F	39	20.3
5	F	23	21.8
11	F	30	21.3
20	M	22	21.0
22	F	19	22.1
25	M	19	22.1
26	F	23	24.5
29	M	30	20.9
Mean		25.9	21.8

Nondiabetic (ND2)			
ID	Sex	Age	BMI
30	F	28	32.9
36	M	39	34.6
37	F	62	21.5
38	F	50	39.9
39	M	51	26.6
43	F	58	29.1
		48	30.6

Noninsulin-Dependent Diabetic Subjects (NIDDM)

Three male and 6 female NIDDM subjects participated in the study with a mean age of 51.9 years (range: 32 - 64) and an average BMI of 29.5. Mean duration of diabetes at diagnosis was 5.3 years. As indicated by their HbA1c levels, M = 6.5 (range: 5.1 - 8.5), subjects displayed a varied range of diabetic control with most subjects evidencing normal to mild hyperglycemia for the month prior to participating in the study. Although most of these subjects used oral hypoglycemic agents (third generation glyburides), 3 of the 9 NIDDM subjects relied solely on diet to control their diabetes. See Table 1 for detailed individual data on these subjects.

Nondiabetic Control Subjects (NC)

A total of 16 nondiabetic control subjects (9 female and 7 male) participated in the study. A subset of these subjects (n = 10) closely matched the IDDM group (mean age: 25.9 years; mean BMI: 21.8) while the remainder of the subjects (n = 6) matched the NIDDM subjects (mean age: 48 years, mean BMI: 30.6). Refer to Table 1 for individual data.

Manipulation Checks

Self Report Mood Measures

Before examining the effect of the stressor condition on blood glucose, pre- to post-stress mood data were examined to determine if subjects in fact reported mood changes consistent with the stress manipulation. Pre-post change scores for the State portion of the STAI and each of the dimensions of the SAM for each of the two experimental days were analyzed using a repeated measures ANOVA with one between subjects' factor (Group: IDDM/NIDDM/Nondiabetics), and one within subjects' factor (Condition: Stress/Control) to test the effect of the stressor on mood.

No significant differences were found between the three groups on any of the self-report measures. Mood changes were associated with significantly less pleasure, greater anxiety and less feeling of control on the SAM and greater state anxiety on the STATE for the stress condition. See Figures 1 and 2 for groups means by condition on each measure. The greater the negative change score the more unhappiness, anxiety, and less feeling of control indicated compared to baseline.

These observations are supported by the following statistics. A main effect for condition on each of the dimensions of the SAM was found. Pleasure: $F(1,31) = 16.00$, $p < .0004$; Anxiety: $F(1,31) = 35.91$, $p < .0001$; and Control: $F(1,31) = 24.25)$, $p < .0001$. Consistent with these

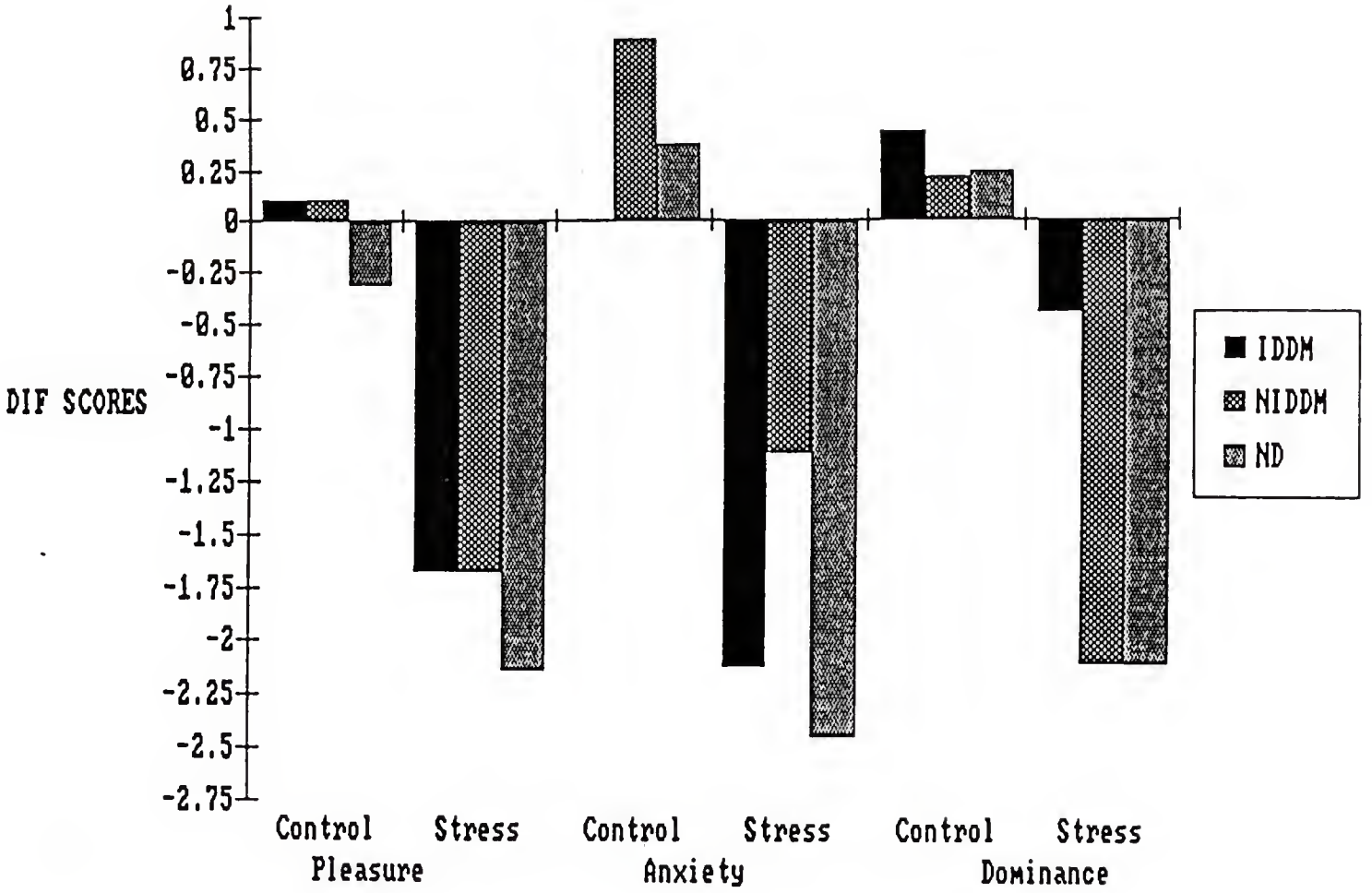

Figure 1. Self-Assessment Manikin difference scores for each group in stress and control conditions.

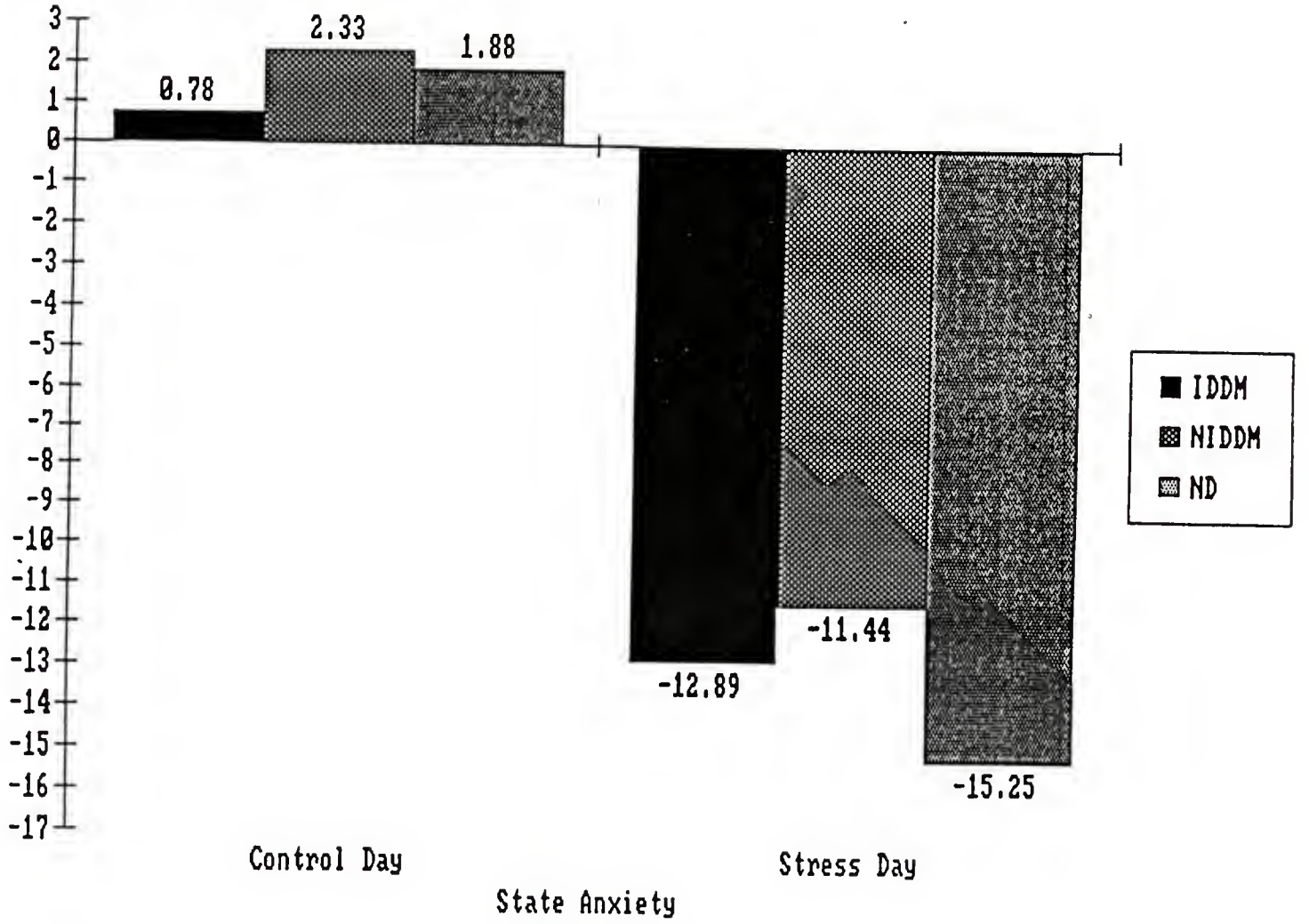

Figure 2. State anxiety difference scores for each group in stress and control conditions.

findings, a significant main effect for condition on the STATE was evident $F(1,31) = 39.23$, $p < .0001$.

Heart Rate

Figure 3 presents the changes in heart rate that occurred during the study. As expected, heart rate increased significantly during the stressor for all groups. In the stress condition, heart rate increased from an average of 70 beats per minute (BPM) during the baseline to an average of 78 BPM during the stressor and remained elevated for the full 30 minutes of the stressor before returning to an average post stress mean of 72. In the Control condition, heart rate was low throughout: 69 BPM during baseline, 70 during the stress phase and 72 during the post stress phase.

To permit data analyses, heart rate was averaged over 10 minute intervals throughout the study. The two 10 minute baseline intervals were then combined for each subject on each experimental day to form a mean baseline heart rate. Similarly, the three intervals during the stress phase were combined to establish a mean stress heart rate. The remainder of the intervals after the stress phase were incorporated to form a mean post stress heart rate.

A repeated measures ANOVA with one between subjects' factor (Group: IDDM/NIDDM/Nondiabetics) and two within subjects' factors (Condition: Stress/Control and Phase:

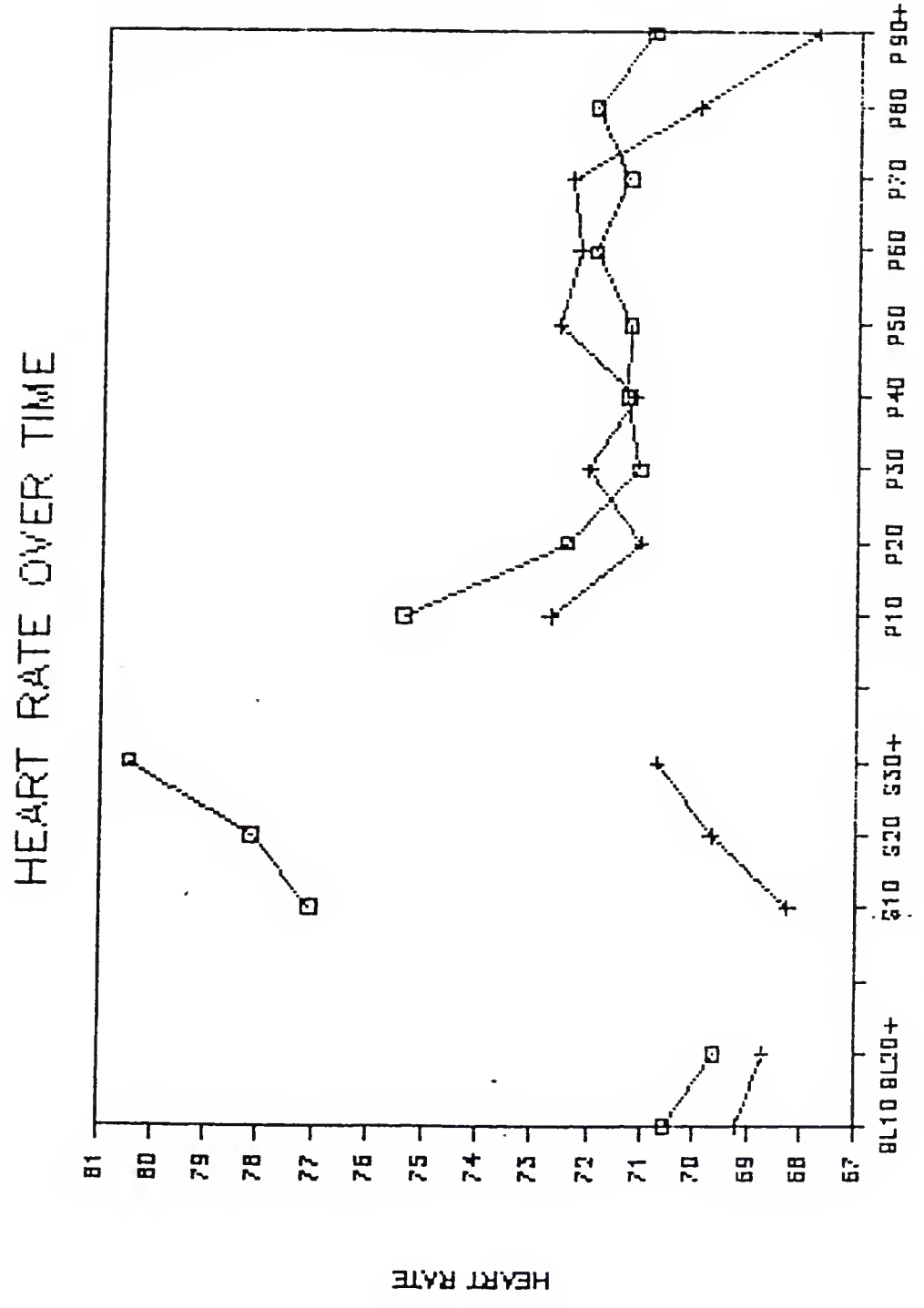

Figure 3. Heart rate over time for all subjects during stress and control conditions.

Baseline/Stress/Poststress) was utilized to determine the effects of the stressor on heart rate. As expected, the heart rate data showed a highly significant main effect for Condition, $F(1,31) = 24.02$, $p < .0001$, Phase, $F(2, 62) = 19.44$, $p < .0001$ and a significant interaction of Condition and Phase, $F(2,62) = 44.13$, $p < .0001$, confirming the effect of the stressor. There was no main effect found for group, suggesting that all groups had similar cardiovascular responses to the stressor. Subsequent analyses by phase reveal a significant main effect for Condition during the Stress phase (with heart rate being greater on the stress day compared to the control day), $F(1,31) = 44.87$, $p < .0001$, but not during Baseline or Poststress phases.

Blood Cortisol

Figure 4 presents the changes in cortisol levels that occurred during the study. As expected, plasma cortisol levels were relatively higher during the stressor and gradually returned to levels similar to post stress levels on the control day. A repeated measures ANOVA was computed for blood cortisol with one between subjects' factor: Group (IDDM/NIDDM/Nondiabetics) and two within subjects' factors: Condition (Stress/Control), and Time (measurement periods: 1-10). As expected, there was a significant main effect for Condition, $F(1,28) = 9.00$, $p < .0027$, Time, $F(9,252) = 7.06$,

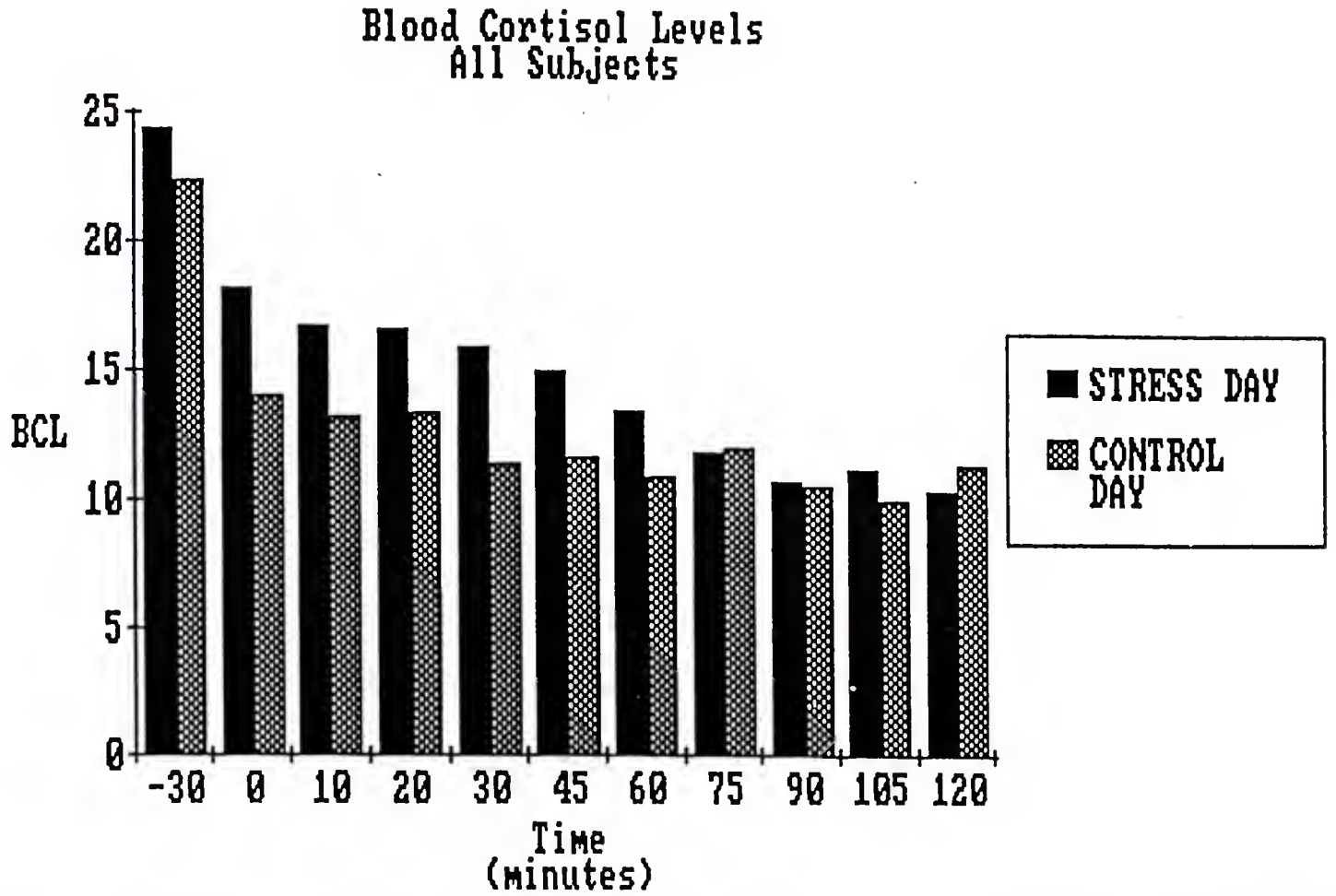

Figure 4. Plasma cortisol levels (with p values) for all subjects in stress and control conditions

$p < .0001$, and a Time by Condition interaction $F(9,252) = 2.80$, $p < .0068$. No group differences were detected.

Subsequent analyses revealed significant differences at times 0: $F(1,33) = 5.04$, $p < .0316$, 10: $F(1,33) = 7.49$, $p < .0099$, 20: $F(1,32) = 12.49$, $p < .0013$, 30: $F(1,32) = 15.88$, $p < .0004$, 45: $F(1,32) = 8.35$, $p < .0069$, 60: $F(1,33) = 4.23$, $p < .0477$.

Blood Glucose

As expected, subject groups entered the study with significantly different baseline levels of blood glucose, $F(2,31) = 16.14$, $p < .0001$ on the stress day, and $F(2,31) = 31.52$, $p < .0001$ on the control day, with the IDDM subjects showing the highest levels. The following baseline blood glucose levels (mg/dl) by group and condition were found: IDDM: stress day = 245, control day = 220; NIDDM: stress day = 161, control day = 160; Nondiabetics: stress day = 94, control day = 93. In order to control for these differences and to permit a fair comparison, the blood glucose levels were analyzed using difference scores; each data point was subtracted from the subject's baseline blood glucose level. Additionally, in order to look at the data from another perspective, percent change scores were used to analyze the blood glucose data; each data point was subtracted from the subject's baseline blood glucose level,

and then divided by the baseline blood glucose level. The results of these analyses were essentially identical to the results when using difference scores and, therefore, will not be reported in this text. Table 2 displays actual data for IDDM and NIDDM blood glucose. Individual subject graphs are presented in Appendix E.

Variability

Between-group tests of differences in blood glucose variability were performed. Relevant analyses involved assessing the standard deviation and range of blood glucose levels.

The standard deviation of blood glucose difference scores for each subject was calculated for each condition (stress and control). A repeated measures ANOVA of the standard deviation data was performed with one between subjects' factor: Group (IDDM/NIDDM/Nondiabetic) and one within subjects' factor (Condition: Stress/Control). A significant main effect for Group was revealed, $F(2,31) = 8.78$, $p < .001$, with IDDM showing the greatest variability. The following mean standard deviations by group were found: IDDM = 28.8, NIDDM = 20.4, Nondiabetics = 13.6. There were no significant differences between the Stress and Control conditions.

Table 2. IDDM and NIDDM Blood Glucose Data for Control Day

	BL	IDDM								
		Difference Score/% Change								
ID	BGL	10	20	30	45	60	75	90	105	120
Control Group										
9	159	1.5/9.4	25.5/16	14/8.8	3.5/2.2	12.5/7.9	25/15.7	41.5/26.1	28/17.6	61.5/38.7
12	171.5	7.5/4.4	8.5/5.0	39/22.7	46.5/27.1	56/32.7	34.5/20.1	15.5/9.0	-4/-2.3	-22.5/-13.1
14	201	-43/-21.4	-51.5/-25.6	-51/-25.4	-61/-30.3	-46.5/-23.1	-50/-24.9	-51/-25.4	-53.5/-26.6	-63.5/-31.6
15	350	-.5/-.1	22.5/6.4	25.5/7.3	48.5/13.8	24.5/7	7.5/2.1	-22.5/6.4	-51.5/-14.7	-64.5/-18.4
16	292	0/0	-2.5/.8	3.5/1.2	11/3.8	14.5/5	2.5/.8	-6.5/-2.2	-2.0/-.7	-15/-5.1
18	354	-37/-10.5	-11.5/-3.3	-17/-4.8	-22/-6.2	-51.5/-14.5	-49.5/-14	-43.5/-12.3	-32.5/-9.2	-24/-6.8
19	186	1/.5	0/0	19.5/10.5	18/9.7	32/17.2	46.5/25	67.5/36.2	64/34.4	60/32.2
21	212.5	-17./-8	-42.5/20	-36/-17	-62/-29.2	-50.5/-23.7	-64.5/30.3	-104.5/-44.2	-121.5/-57.2	-139.5/-65.6
40	215	12/5.6	38/17.7	84.5/39.3	103/48	125/58.1	147/68.4	168.5/78.4	160/74.4	147/68.4
Stress Group										
9	156	-14.5/-9.3	-23/-14.7	-31/-19.9	-39.5/-25.3	-33.5/-21.5	-33/-21.2	-28/-17.9	-22.5/-14.4	-30/-19.2
12	223.5	-8/-3.6	-7.5/-3.4	-7/-3.1	37/16.5	71/31.8	63/28.2	43/19.2	16/7.1	4.5/2.0
14	260	-1/-.3	-19/-7.3	-28/-10.8	-42.5/-16.3	-57/-21.9	-75.8/-29	-95/-36.5	-118.5/-45.6	-127.5/-49
15	379.5	-16/-4.2	-15/ -3.9	-10./5-2.8	63/16.6	80/21	57/15	19.5/5.1	-7.5/-2	-46.5/-12.3
16	74	-18/-24.3	-10/-13.5	-4.5/-6.1	11.5/15.5	21/28.4	25/33.8	22.5/30.4	19.5/26.3	6.5/8.8
18	352.5	-24/-6.8	-37/-10.5	-27.5/-7.8	-13/-3.7	-18.5/-5.2	-12.5/-3.5	-19.5/-5.5	7/2	-9/-2.5
19	223	-7.5/-3.4	10.5/4.7	23.5/10.5	39/17.5	70.5/31.6	80.5/36.1	84.5/38	83/37.2	64/28.7
21	173	-28/-16.2	-28.5/-16.5	-11.5/-6.6	3.5/2	8/4.6	-28/-16.2	-39.5/22.8	-72/-41.6	-96/-55.5
40	199	-8/-4	4.5/2.3	31.5/15.8	65/32.7	107/53.8	89/44.7	147.5/74.1	147.5/74.1	135.5/68.1

Table 2. Continued

NIDDM

ID	BL BGL	Difference Score/% Change 10	20	30	45	60	75	90	105	120
Control Group										
13	242.5	0/0	0/0	20.5/8.5	36/14.8	67.5/27.8	85/35	75/30.9	65/27	52.5/21.6
17	207	7/3.4	17/8.2	30.5/14.7	59.5/28.7	62/30	48/23.2	22/10.6	38/18.3	34.5/16.7
23	160	-17/10.6	-45.5/-28.4	6/3.8	15/9.4	25/15.6	24/15	-8.5/-5.3	-5.5/-3.4	-10/-6.3
28	109.5	-14.5/-13.2	7/6.4	29.5/26.9	34/31.1	34/31.1	41.5/37.9	34/31.1	25.5/23.3	14/12.8
30	102.5	11.5/11.2	20.5/20	32/31.2	42/41	49.5/48.3	59/57.6	53.5/52.2	52.5/51.2	35/34.1
31	136	-1.5/-1.1	7.5/5.5	0/0	17/12.5	42.5/31.3	41.5/30.5	53.5/39.3	35/25.7	33/24.3
32	152.5	8/5.2	10/6.6	35.5/23.3	52.5/34.4	43/28.2	34/22.3	8.5/5.6	13.5/8.9	-2/-1.3
35	164.5	12/7.3	25.5/5.5	49.5/30.1	86.5/52.6	105.5/64.1	114.5/69.6	9.4/57.1	88.5/53.8	89.5/54.4
42	174.0	18/10.32	37/21.3	55.5/31.9	72/41.4	67/38.5	52/29.9	38.5/22.1	21.5/12.4	7.5/4.3
Stress Group										
13	227	28/12.3	44.5/19.6	71/31.3	87.5/38.5	109.5/48.2	83/36.5	75.5/33.3	58.5/25.8	47.5/20.9
17	214	4/1.9	15/7	13/6.1	40/18.7	48/22.4	55/25.7	39.5/18.5	35.5/16.6	23.5/11
23	159.5	25.5/16	20/12.5	27.5/17.2	57.5/36.1	68.5/43.9	65/40.8	12.5/7.8	11.5/7.2	12/7.5
28	105.5	-2/-1.9	7.5/-7.1	17.5/16.6	33.5/31.8	32/30.3	21.5/20.4	19.5/18.5	24.5/23.2	11.5/10.9
30	114.5	18.5/16.2	39.5/34.5	52/45.4	56.5/49.3	55.5/48.5	56/48.9	47.5/41.5	49.5/43.2	26/22.7
31	120.5	9/7.5	28/23.2	33.5/27.8	23/19.1	5.5/4.6	3.5/2.9	17.5/14.5	16/13.3	14/11.6
32	162	20/12.3	25/15.4	31.5/19.4	40.5/25	20/12.3	5.5/3.4	11/6.8	-11/-6.8	-2/-1.2
35	162.5	20/12.3	51/31.4	69/42.5	82/50.5	66.5/40.9	72.5/44.6	63.5/39.1	58-35.7	54.5/33.5
42	172.5	8.2/4.8	14.7/8.5	36.2/21	69.2/40.2	73.2/42.5	51.2/29.7	32.2/18.7	14.2/8.2	-3.3/-1.9

Range. Range was calculated by subtracting the minimum blood glucose level attained from the maximum blood glucose level attained per subject for each condition. A repeated measures ANOVA of range with one between subjects' factor (Group: IDDM/NIDDM/Nondiabetic) and one within subjects' factor (Condition: Stress/Control) was performed on the blood glucose range data. A significant main effect for group $F(2,31) = 11.70$, $p < .0002$ was found with IDDM again showing the greatest range. The following mean ranges by group were found: IDDM = 88, NIDDM = 66.5, Nondiabetics = 38.8. No significant differences between conditions (stress vs control) occurred.

Despite evidence of heterogeneity of variance, the F test statistic is expected to be robust given the small sample size. Only minimal inflation of the probability of rejecting the null hypothesis (Type 1 error) is expected.

Experimental Effects

Within-Subject Comparisons

In order to determine the effects of the experimental manipulation on blood glucose reactivity, a repeated measures ANOVA with 2 within subjects' factors: Condition (Stress/Control) and Time (measurement periods: 1 - 9) was computed using blood glucose difference scores.

Nondiabetics

As seen in Figure 5, unstressed nondiabetic subjects showed an expected peak and recovery of blood glucose following the Sustacal load. Relative to this baseline, on the stress day a similar peak was seen but delayed for 25 minutes. Thus, a significant main effect for Time was noted, $F(8,120) = 8.70$, $p < .0001$ and a significant Time by Condition interaction $F(8,120) = 6.92$, $p < .0001$. Subsequent analyses examined the differences between the Stress versus Control condition at each point in time. Results indicate differences in blood glucose at 5 of the 9 points in time, at time 10: $F(1,15) = 2.77$, $p < .12$, 20: $F(1,15) = 10.26$, $p < .006$, 45: $F(1,15) = 6.83$, $p < .02$, 60: $F(1,15) = 8.46$, $p < .011$, 75: $F(1,15) = 3.64$, $p < .076$, and 90: $F(1,15) = 4.21$, $p < .058$ minutes after the Sustacal load. On stress days, blood glucose peaked at 20 minutes after the Sustacal, while on control days the blood glucose peaked at 45 minutes. This denotes a 25 minute delay in the blood glucose peak on stress days compared to nonstress days. This pattern was exhibited by 11 of 16 subjects (see Table 1 for individual data).

These results are very similar to the Wing et al. (1985) data (Figure 6) which shows a glucose peak at 30 minutes after the carbohydrate load on the stress day, with a 30 minute shift on the control day with glucose peaking at 60 minutes.

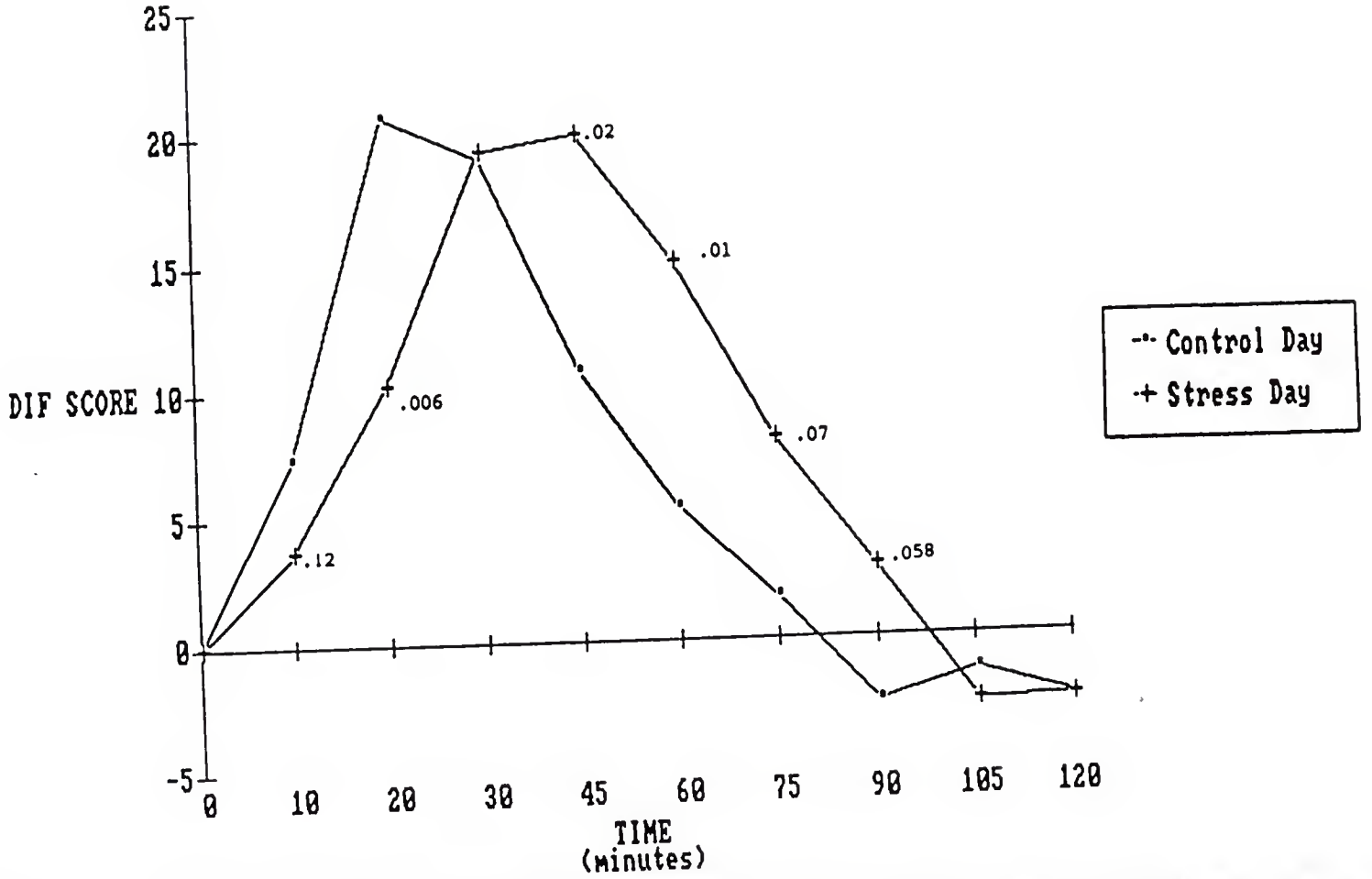

Figure 5. Blood glucose difference scores (with p values) for nondiabetic subjects after the Sustacal load in stress and control conditions.

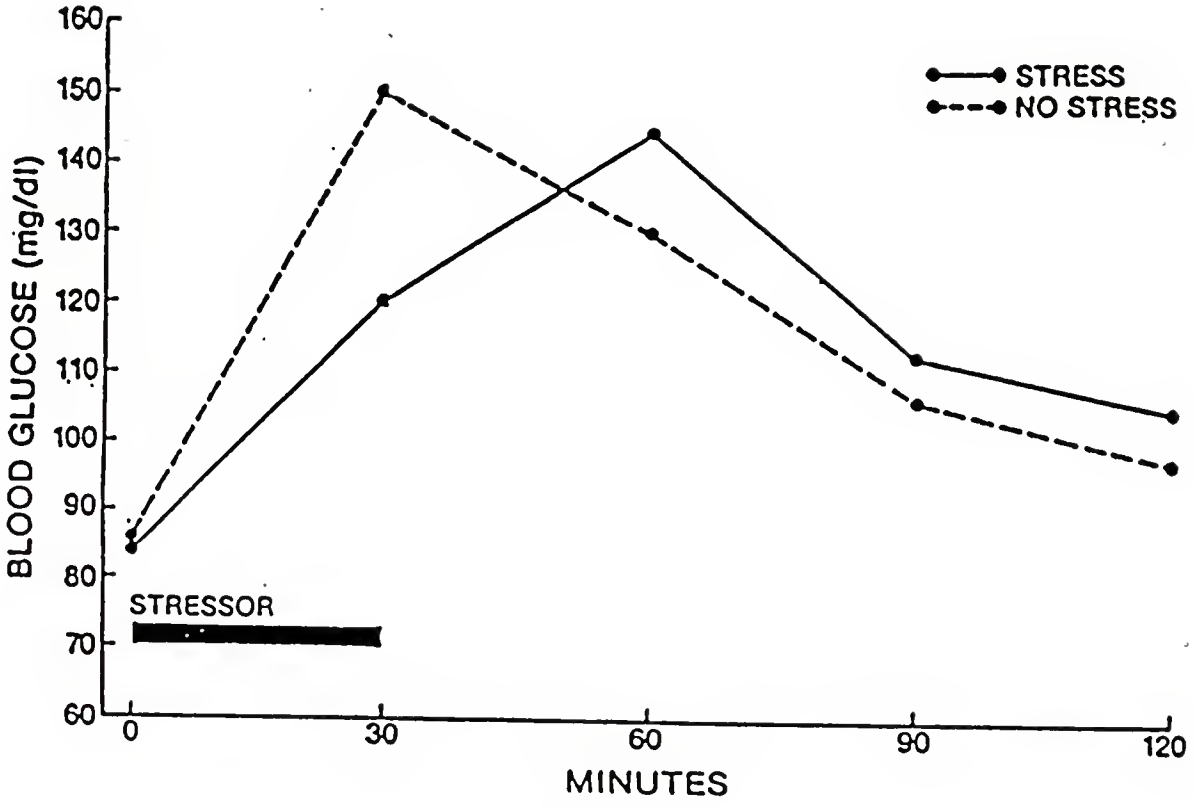

Figure 6. Blood glucose levels measured 0, 30, 60, 90, and 120 minutes after Polycose load in stress and non stress conditions.

A repeated measures ANOVA, comparing the two subgroups of the nondiabetics, was computed. In addition to the two within subjects factors (Condition and Time), Subgroup (ND1/ND2) was added as a between subjects factor: the subjects matched with the IDDM subjects (ND1) and the subjects matched with the NIDDM subjects (ND2) (who tended to be older and heavier). As seen in Figure 7, the pattern of stress effects was similar for each subgroup but ND2 subjects had higher blood glucose levels throughout the study than did ND1 subjects. This is confirmed by the statistical results which show that in addition to a main effect for Time, $F(8,112) = 11.11$, and the expected Time by Condition interaction, $F(8,112) = 6.21$, $p < .0003$, there was a significant main effect for Subgroup $F(1,14) = 10.45$, $p < .006$.

IDDM

Figure 8 clearly shows that blood glucose dropped significantly during the first 30 minutes (Stress Phase) on the stress day before peaking abruptly at time 60. There were no main effects for Condition or for Time but the Time by Condition interaction was highly significant, $F(8,64) = 6.09$, $p < .0016$. Subsequent analyses indicate that differences in blood glucose levels were evident at times 10: $F(1,8) = 9.86$, $p < .012$, 20: $F(1,8) = 7.40$, $p < .03$, 30: $F(1,8) = 6.10$, $p < .04$, and 105: $F(1,8) = 3.45$, $p < .10$.

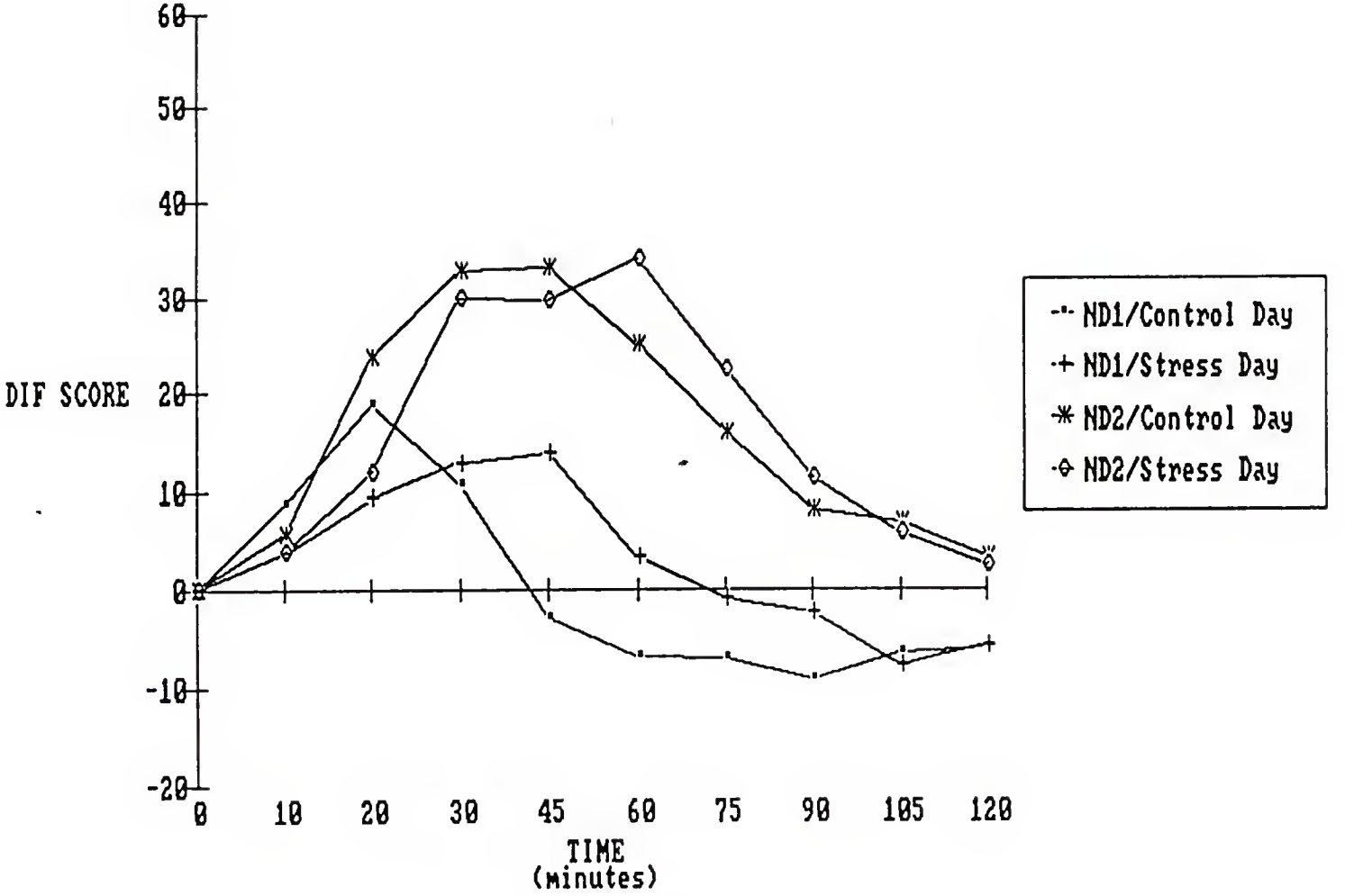

Figure 7. Blood glucose difference scores for nondiabetic subjects separated into IDDM matched subjects (ND1) and NIDDM matched subjects (ND2) in stress and control conditions.

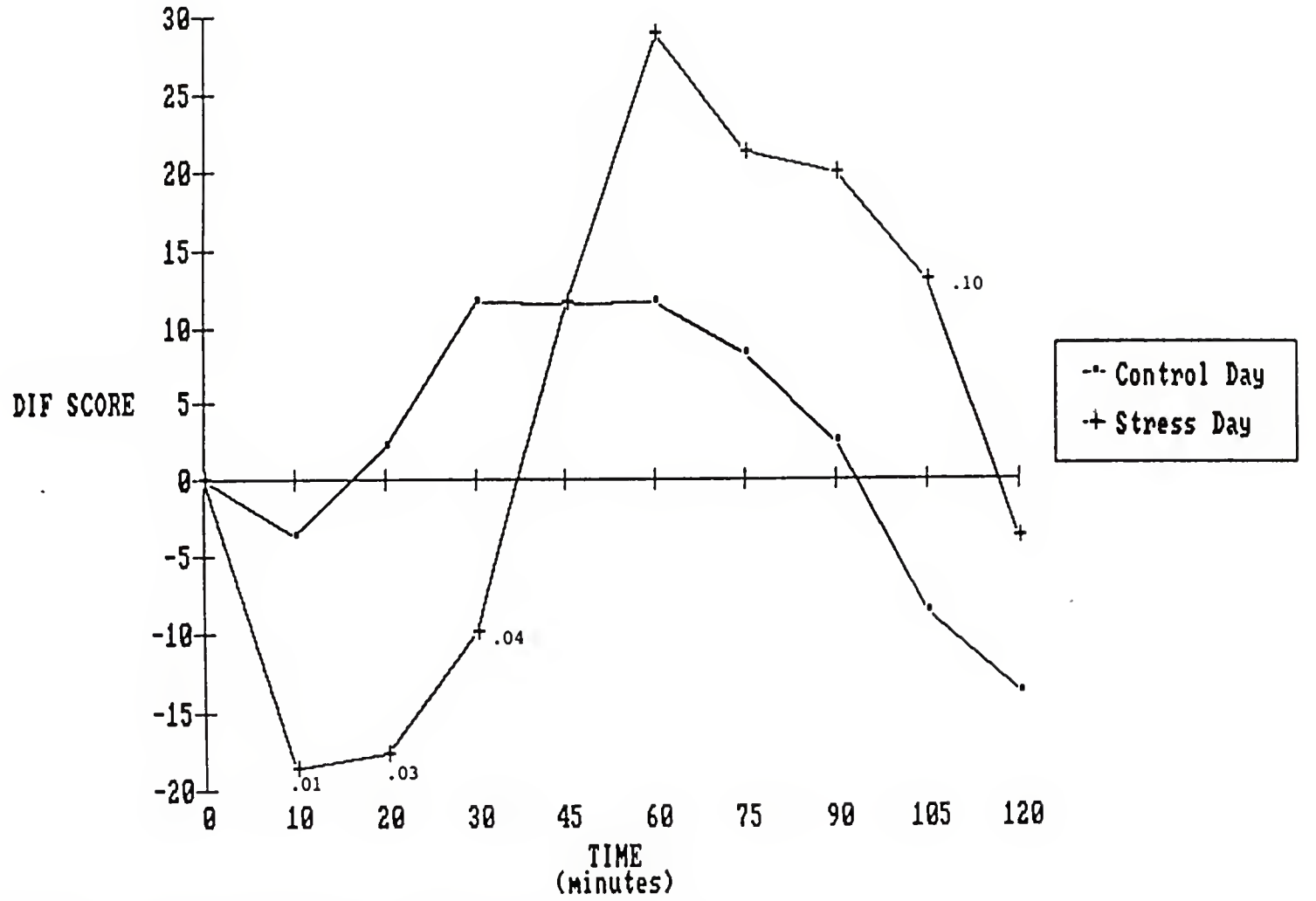

Figure 8. Blood glucose difference scores (with p values) for IDDM subjects after the Sustacal load in stress and control conditions.

Eight of the nine IDDM subjects showed this general pattern of decreased blood glucose during the stressor, followed by an increase. One evidenced a decrease in blood glucose during the stressor that continued to decline throughout the study. See Table 2 for actual data and Appendix E for individual subject graphs.

NIDDM

As seen in Figure 9, blood glucose tended to rise sooner on stress days and peaked at time 45, while on control days, the peak shifted approximately 30 minutes, to time 75.

In addition to a main effect for Time, $F(8,64) = 15.21$, $p < 0001$, there was a significant Time by Condition interaction, $F(8,64) = 3.99$, $p < .015$. Subsequent analyses show blood glucose differences at times 10: $F(1,8) = 5.34$, $p < .05$, 20: $F = (1,8) = 4.58$, $p < .065$ and 105: $F(1,8) = 3.31$, $p < .10$.

Two of the nine NIDDM subjects did not exhibit the general pattern described above. Close inspection of these two subjects (#17 and # 42) reveals interesting findings. As seen in Table 3, subject #17, who showed an opposite pattern, was the only subject to report more positive mood changes post stress compared to the control day. Subject #42 who did not show much of an effect at all was the only subject on heart medication (50 mg Cardizam).

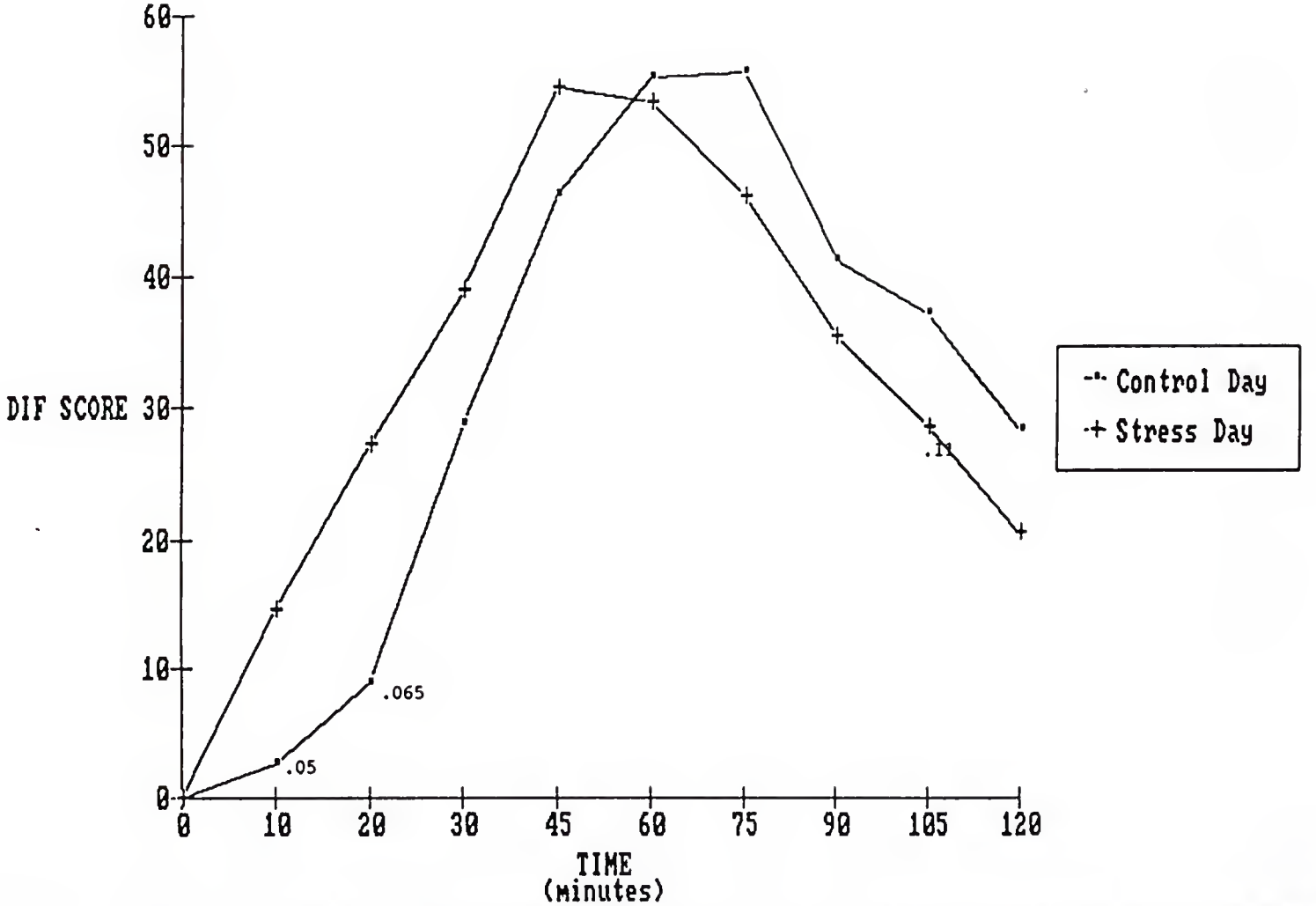

Figure 9. Blood glucose difference scores (with p values) for NIDDM subjects after the Sustacal load in stress and control conditions.

Table 3. Combined Self-Report Diff Scores

Subject ID	Control Group Diff Scores	Stress Group Diff Scores
IDDM		
9	0	-9
12	1	-46
14	2	-10
15	8	-39
16	2	-17
18	0	-11
19	3	-2
21	6	-18
NIDDM		
13	11	-6
17	0	9
23	-7	-15
28	-1	-25
30	-7	-19
31	-1	-8
32	-3	-1
35	-3	-29
42	1	-48

Between Group Comparisons

A repeated measures ANOVA was computed for blood glucose difference scores with one between subjects' factor: Group (IDDM/NIDDM/Nondiabetics) and two within subjects' factors: Condition (Stress/Control), and Time (measurement periods 1 - 9). Results show a significant Group by Condition by Time interaction, $F(16,248) = 7.91$, $p < .001$, with a main effect for Group $F(2,31) = 3.78$, $p < .034$, and a significant Group by Time interaction, $F(16,248) = 3.11$, $p < .02$. Further analyses by condition were warranted to analyze the location of the differences.

Control condition

As seen in Figure 10, blood glucose for the NIDDM rose slower than the Nondiabetic group, but ultimately achieved a much higher level (greater difference score). The IDDM blood glucose curve actually dipped slightly (time = 10) before rising by time = 20.

Groups differed within the control condition at times 10: $F(2,31) = 3.06$, $p < .06$, 20: $F(2,31) = 3.09$, $p < .06$, 45: $F(2,31) = 3.79$, $p < .034$, 60: $F(2,31)= 5.85$, $p < .007$, 75: $F(2,31) = 5.58$, $p < .0085$, 90: $F(2,31)= 2.62$, $p < .09$, and 105: $F(2,31) = 2.45$, $p < .10$.

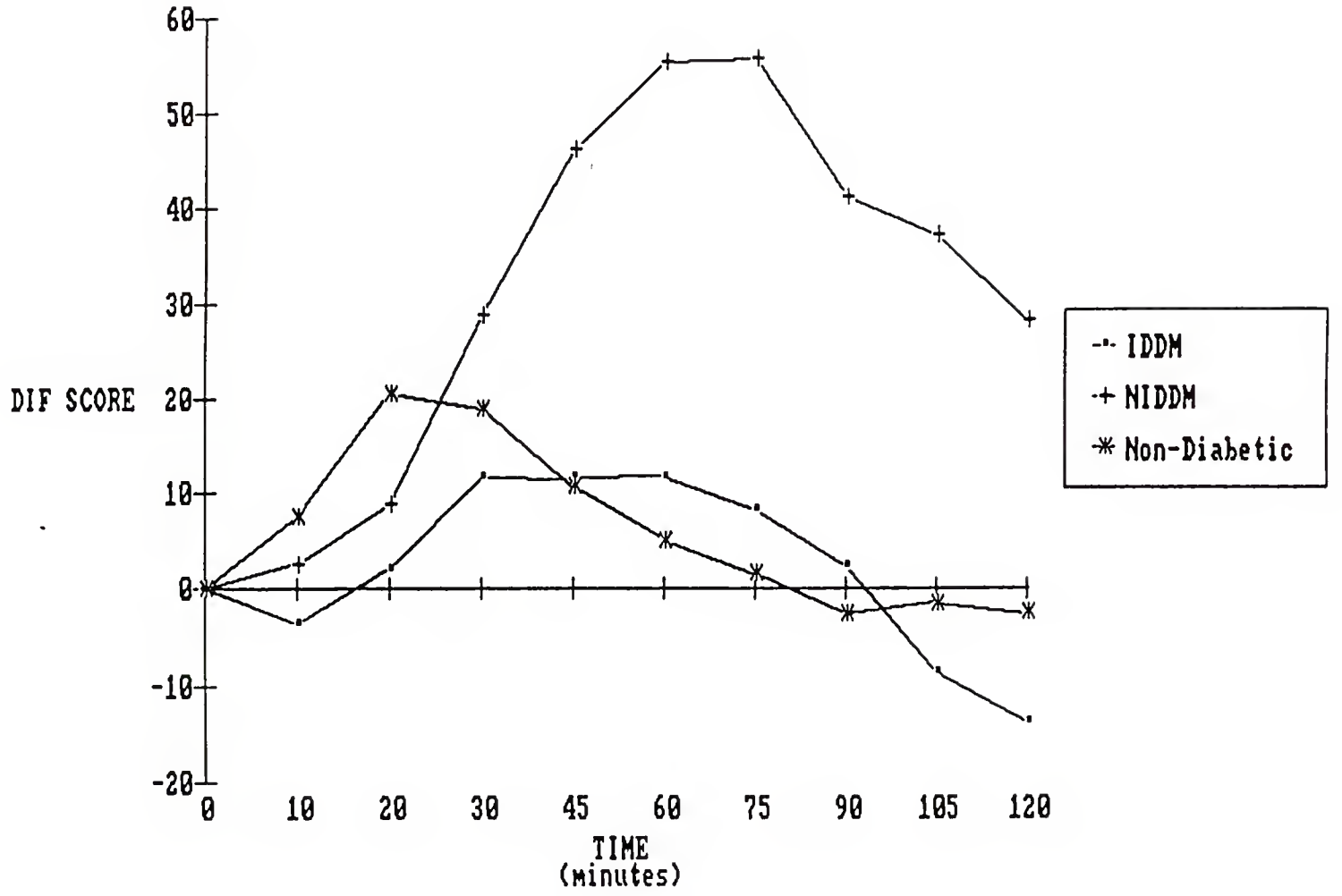

Figure 10. A comparison between all groups (IDDM, NIDDM, and nondiabetic subjects) for the control condition.

Stress condition

There appeared to be greater group differences during the stressor period. As seen in Figure 11, the relative blood glucose rises during the initial (stress) phase for the Nondiabetics and NIDDMs are opposite in the Stress as compared to the Control condition. In other words, the NIDDM curve rose more quickly compared to the Nondiabetic controls during the stress condition, whereas this pattern was reversed on the control day. The IDDM curve dropped even lower than the other two groups during the stress phase on the stress day and rose higher than the nondiabetic controls during the post-stress phase.

Groups differed within the stress condition at times 10: $F(2,31) = 27.19$, $p < .0001$, 20: $F(2,31) = 22.63$, $p < .0001$, 30: $F(2,31) = 15.20$, $p < .0001$, 45: $F(2,31) = 6.24$, $p < .005$, 60: $F(2,31) = 3.21$, $p < .054$, 75: $F(2,31) = 3.51$, $p < .042$.

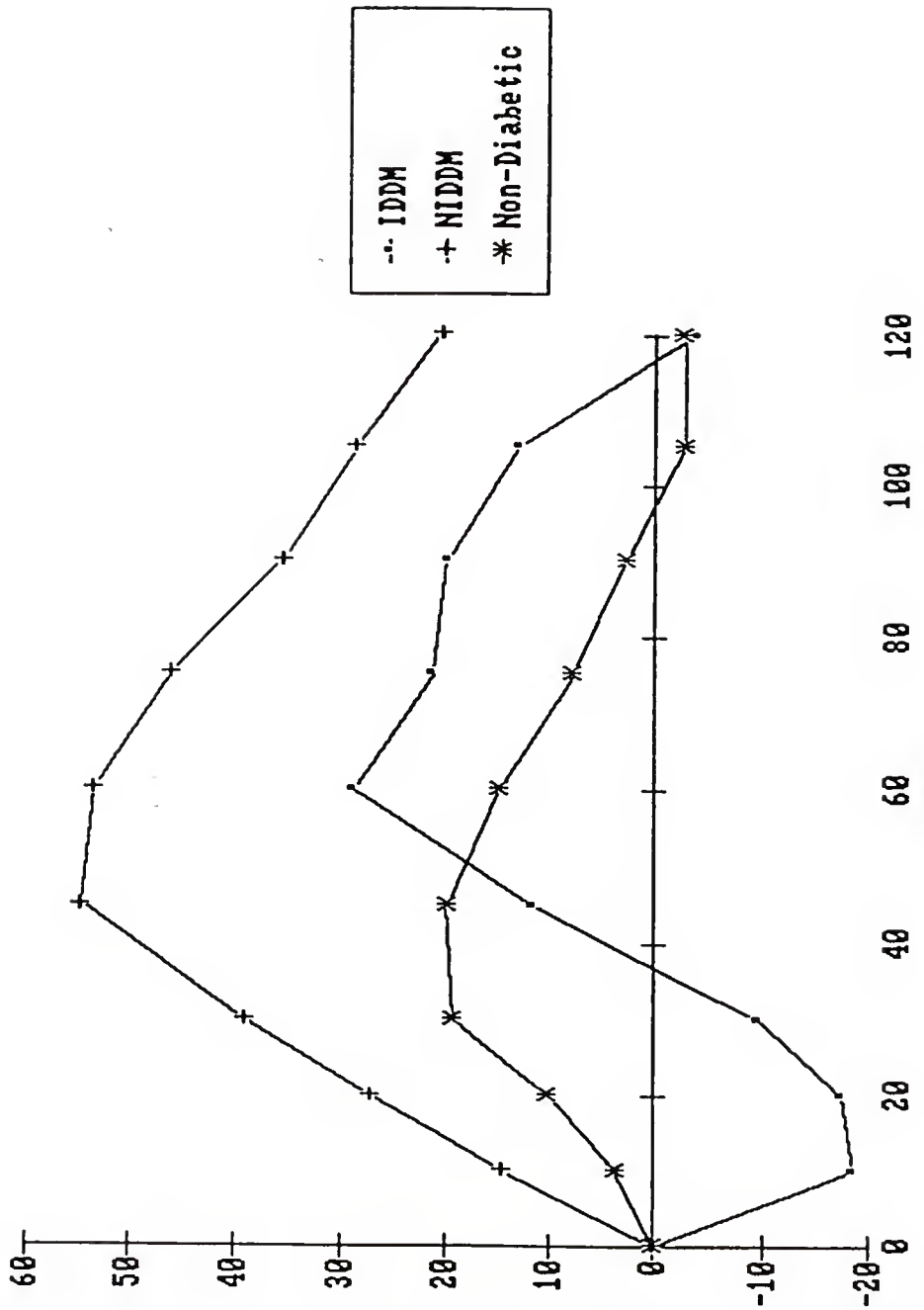

Figure 11. A comparison between all groups (IDDM, NIDDM, and nondiabetic subjects) for the stress condition.

CHAPTER 4
DISCUSSION

This study provides insight into the effects of psychological stress on blood glucose levels of IDDM and NIDDM subjects. The results help to reconcile previous conflicting data on this subject and build upon the recent work of Wing et al. (1985) with nondiabetics. The results obtained here are believed to be of particular value and interest because of the methodology utilized. Specifically, this study utilized a standardized psychological stressor, provided multiple measurements of dependent variables, and used a repeated measures design in which each subject was studied twice, serving as their own control. The stressor effectively induced emotional arousal in all groups as evidenced by significant increases in cardiovascular arousal, stress hormone production, and subjective ratings of emotional arousal.

The findings suggest that, for both diabetic and nondiabetic subjects, performance of the 30 minute stressor during the stress day resulted in a significant change in blood glucose compared to the control day, demonstrating that even a relatively short exposure to a moderately stressful event can cause metabolic disruption. However,

the nondiabetic, IDDM, and NIDDM groups studied displayed a different pattern in response to the experimental manipulation. In nondiabetics, stress affected glucose metabolism by delaying the peak of the glucose curve about 25 minutes compared to the control day. Subjects with NIDDM showed a shift of the glucose peak in the opposite direction from the nondiabetics. Subjects with IDDM showed yet a different pattern with an initial decrease in blood glucose during the stressor followed by an abrupt increase following termination of the stressor.

The current study reveals that inconsistencies in the results of previous studies may be attributable to an insufficient number of blood glucose measurements over time. The results obtained here clearly demonstrate that blood glucose level is a very dynamic variable and that the direction of blood glucose change depends on when the blood samples are taken and when the psychologic stressor is administered in relationship to the last meal. For example, if in the present study, blood had been taken only at baseline and at 20 minutes for the IDDM and nondiabetic subjects, the investigator would have concluded that blood glucose levels were lower during stress than nonstress. However, if only a 60 minute sample had been taken, blood glucose levels would have appeared higher in response to stress. At time 30 for nondiabetic subjects or time 45 for IDDM subjects there would have appeared to be no change.

These conclusions would have misrepresented the actual effect of the stressor on glucose levels. Similar spurious results would have been obtained for the NIDDM group. The variability of blood glucose over time necessitates frequent measurement in order to get an accurate portrayal of the effect of stress on blood glucose. Hence, this methodological study was successful in helping to clarifying the nature of the inconsistencies in the literature.

Comparison to the Wing Study: Nondiabetic Controls

The present study essentially replicates the results of the Wing et al. (1985) study showing that acute psychological stress delays the peak glucose response in nondiabetic subjects following a glucose load (Figure 4 and Figure 5). However, the design of the present study, which allowed for more frequent, painless blood sampling, revealed additional information regarding the shape of the blood glucose curves. For example, in the nondiabetic group blood glucose peaked at time = 20 on the control day. If the same measurement times as in the Wing study were used, this earlier glucose peak would have been missed. Similarly, the glucose peak on the stress day occurred at time = 45 in the present study, whereas Wing et al. (1985) did not pick up the peak until time = 60 as they did not measure blood glucose at time 45. The additional information gleaned from more frequent blood glucose measurement particularly during

the stress phase becomes even more important when comparing the two control groups and is crucial when assessing blood glucose change in the IDDM and NIDDM groups.

Unlike the Wing et al. (1985) study, which used only young, lean subjects, the present study included nondiabetic subjects to match the NIDDM subjects who tended to be older and heavier. Although the general pattern of response to the experimental manipulation was similar, the nondiabetic subjects matched to the NIDDM subjects in general attained a higher blood glucose level and slower return to near baseline levels (Figure 7). The differences in the blood glucose curves are likely due to the impairment of glucose tolerance with age and obesity (Jackson, 1990). When analyzing the blood glucose data of the nondiabetic group by dividing the subjects by age (> 40 years) and then by BMI (> 26), a significant difference was noted for age but not for BMI. Hence, the age variable is likely to be more powerful in accounting for the difference observed in the nondiabetic subgroups.

According to a recent study by Jackson (1990), there is a progressive reduction of glucose tolerance with age. Jackson reports that age-related glucose intolerance is a specific phenomenon distinct from obesity and NIDDM. Impairments in glucose-induced insulin secretion and insulin action are characteristic. The defect in insulin action, after glucose ingestion, is in the delayed suppression of

hepatic glucose production and a delayed rise in insulin mediated glucose uptake. The most predominant disturbance appears to be impaired glucose uptake with skeletal muscle as the principal site of this defect. Because insulin receptors are unchanged with age, the impairment in insulin action is primarily due to a postreceptor defect.

In nondiabetic subjects, acute psychological stress appears to delay the peak glucose response by approximately 25 minutes following a Sustacal load (Figure 4). It appears that stress alters the subject's ability to absorb a liquid meal. There were no differences in the maximum plasma glucose levels attained; thus stress did not raise or lower the ultimate blood glucose peaks, but rather caused a temporal shift in the glucose curve. As proposed in the Wing et al. (1985) study, this shift may be due to slower absorption of glucose. It is likely that the stress affected blood glucose levels by causing a delay in gastric emptying, and therefore a delay in the peak glucose response. This hypothesis is supported by a study by Thompson, Richelson, and Malagelada (1983) which demonstrated that a 20 minute period of cold stress delayed gastric emptying of a liquid meal relative to a control condition due to inhibition of gastric motility. The design of the study and the results, as shown in Figure 12, are strikingly similar to the present study. The graph shows rates of meal delivery into the duodenum for each condition.

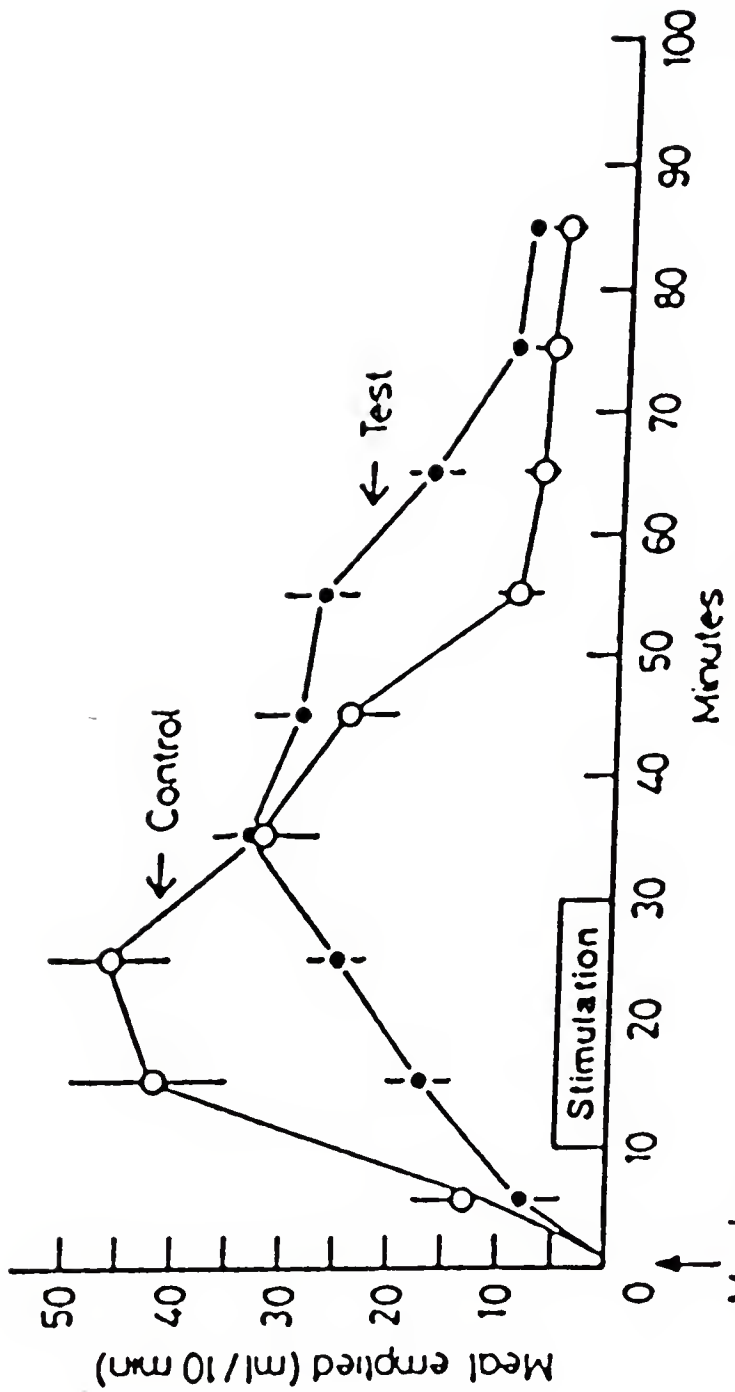

Figure 12. Effect of cold pain on gastric emptying of meal. Rates of meal delivery into duodenum (ml/10 min) during test (cold water) and control (warm water) stimuli are shown. Points represent mean +/- SE (n=9) at each 10 minute sampling period. Meal was ingested at time 0. Stimulations were applied from 10 to 30 minutes postprandially. It is apparent that the test stimulus induces marked delay in rate of gastric emptying of meal relative to control stimulus.

Inhibition of gastric motility by acute stress may occur because of increased sympathetic nervous activity, either by a direct catecholamine effect or indirectly via sympathetic stimulation of glucagon release. Thompson points out that the changes in the autonomic nervous system activity are qualitatively similar to those resulting from other forms of stressful stimulation, including predominantly psychic stimuli such as mental arithmetic.

According to the activities of the sympathetic nervous system on hormone pathways (refer to Figure 13), it is expected that stress may stimulate glucose production by the liver. Such a production is not clearly evident in the results obtained from the controls. It may be that if hepatic glucose production was increased as a result of the stressor, nondiabetics possess such a tight regulatory system that the secretion of insulin counteracted the effects. In addition to responding to glucose, the islet cells in the pancreas respond to a variety of other nonglucose signals (e.g., catecholamines) (Unger & Orci, 1977). In nondiabetics the insulin response to these other signals is modulated by the prevailing glucose level. This regulatory effect of glucose is referred to as potentiation.

IDDM

The results of the study are contradictory to studies reported recently in IDDM literature which found no evidence

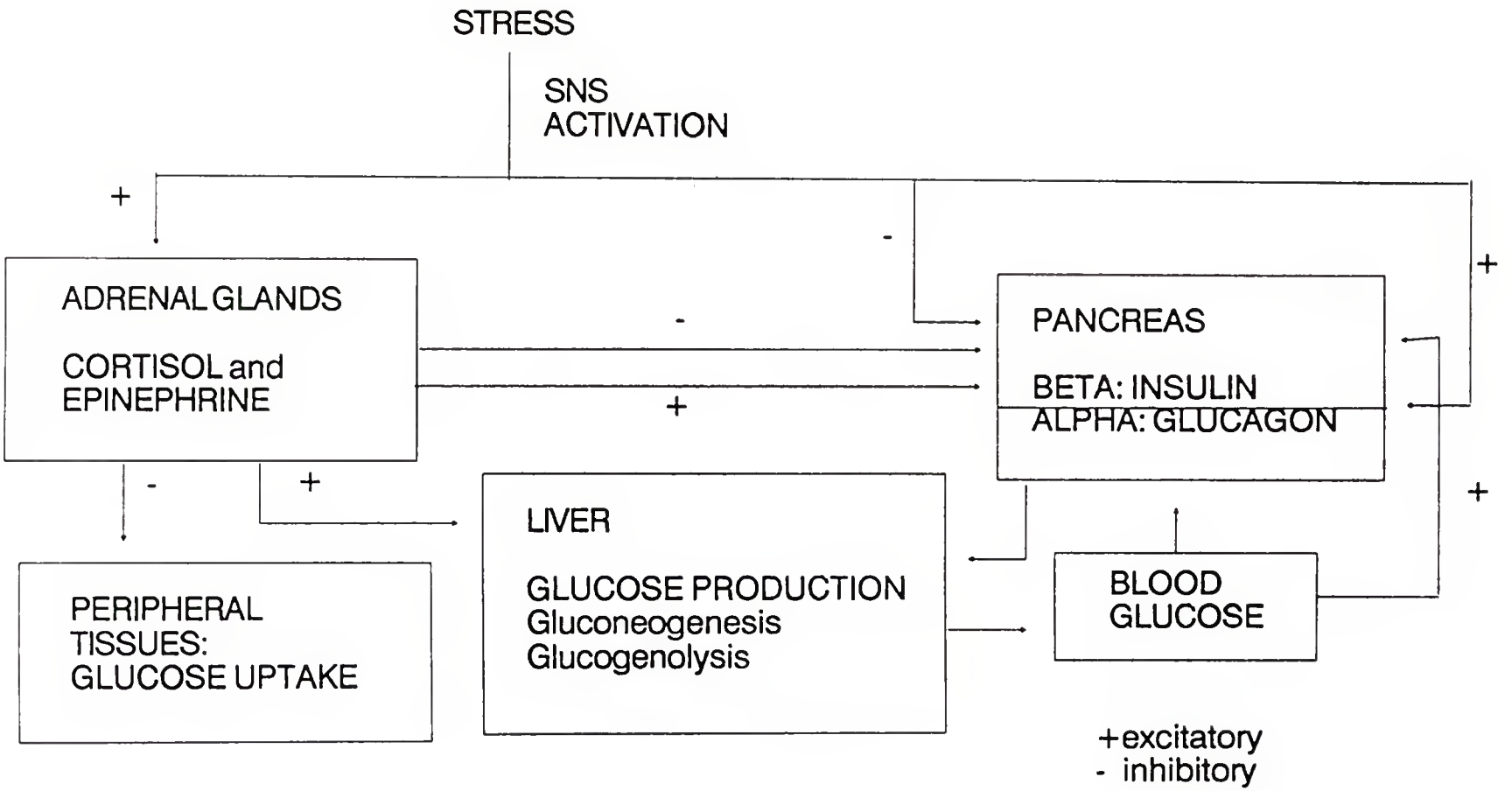

Figure 13. Hormonal and sympathetic nervous system (SNS) effects on blood glucose.

that acute psychological stress has adverse metabolic effects (Kemmer et al., 1986, Delameter, Bubb, Kurtz, Smith, White, & Santiago, 1988; Gilbert et al., 1989), even when stress produced significant increases in cardiovascular responses, subjective ratings of anxiety and significant increases in stress hormone levels. As clearly shown in Figure 8, group blood glucose data for IDDM subjects drops significantly during the stressor period compared to the control condition. This drop is followed by a rapid increase upon completion of the stressor and then a gradual return to near baseline levels by the end of the study period. The pattern may be explained by a combination of the following factors: the insulin injection administered 20 minutes prior to the glucose load; slowed gastric emptying causing delayed glucose absorption; and the effects of sympathetic nervous system activation on hormonal pathways.

It appears that the injected insulin initially causes the blood glucose levels to drop. This lowering of blood glucose levels may be accentuated by slowed gastric emptying which delays the absorption of glucose into the blood. As discussed above, slowed gastric emptying can be expected as a result of the stressor. In response to the stressor and perhaps the sharp drop in blood glucose, counterregulatory hormones (epinephrine and cortisol) or "stress hormones" may be triggered. These "stress hormones" are released into the

blood stream by the adrenal glands. In response to these hormones a number of events may occur which influence the metabolism of carbohydrates and are relevant to circulating glucose level (refer to Figure 13). Glucagon is released into the blood stream by the pancreas, increasing hepatic glucose production (glycogenolysis and gluconeogenesis) and causing glycogen to be converted to glucose by the liver and released into the blood stream. Each of the effects of these stress hormones would tend to raise blood glucose levels. Therefore, a combination of the ingested Sustacal ultimately being absorbed (upon completion of the stressor), and the effect of the stress hormones due to psychic stress and possibly due to a rebound may cause an abrupt rise in the blood glucose level. The severity of the drop and the general shape of the curve for individual subjects are likely to be a function of type and dosage of insulin injected. This important variable may also help explain the great variability in the blood glucose data for IDDM subjects.

On the nonstress day, only a small initial dip in blood glucose level after ingestion of the glucose load is observed. This may be due to the fact that the injected insulin has an available glucose load to act on. Blood glucose slowly rises as ingested glucose is absorbed, levels off and gradually decreases to below baseline level.

A number of studies (e.g., Halter, Beard, & Porte, 1984) show that endogenous epinephrine release or exogenous epinephrine infusion results in exaggerated glycemic response in diabetic patients. This is believed to result from enhanced cortisol and epinephrine-induced glucagon secretion, increased hepatic responsiveness to epinephrine and lack of increased pancreatic insulin secretion. This observation may contribute to the blood glucose increases--particularly in the NIDDM subjects.

NIDDM

These subjects appear to have a slower absorption of ingested glucose compared to the nondiabetics on the control day (refer to Figure 9). This effect may be due to the group's higher mean age and BMI and/or the increased likelihood of gastric stasis with diabetes. However, these subjects ultimately reach a significantly higher blood glucose level and return only halfway to baseline levels at the end of the study. On the stress day their blood glucose level is higher during the stress phase, and peaks at a time earlier than the control day.

This pattern can be explained by the following: unlike the IDDM subjects and nondiabetics, NIDDM subjects do not have a readily available amount of usable insulin to counteract the effects of blood glucose increases due to the stress response described above. Islet cell function

(insulin secretion) in NIDDM is characterized by diminished responses to acute glucose stimulation. Studies show (e.g., Halter & Porte, 1981) that the acute insulin secretory response to IV glucose is markedly impaired in fasting NIDDM patients. In addition, there is an impairment of the potentiating effect of glucose on insulin responses to nonglucose stimuli (e.g. stress hormones). Therefore patients with NIDDM may not be able to augment insulin secretion normally to compensate for the hyperglycemic effects of catecholamines and other stress hormones. Additionally, catecholamines antagonize the ability of insulin to increase glucose utilization (increased insulin resistance) by the peripheral tissues. In other words, these hormones inhibit insulin release from the pancreas and have inhibitory effects on tissues which result in increased resistance to insulin. Thus, the increased blood glucose caused by the sympathetic response to stress may not be utilized by the peripheral tissues until the termination of the stressor. Additionally, there is substantial evidence to support the notion that increased adrenergic sensitivity is a characteristic of NIDDM (Surwit & Feinglos, 1988).

The delayed gastric emptying mechanism may not have nearly as powerful an effect for NIDDM subjects due to the following factors: slowed gastric system in general compared to nondiabetics (Sninsky, 1989); hypersensitivity to catecholamines compared to nondiabetics thereby producing

more glucose by the liver (Halter et al., 1984; Surwit & Feinglos, 1988); inhibition of insulin response during stress superimposed on an already impaired insulin response to increased blood glucose (Halter et al., 1984). Therefore, slowed gastric motility in response to stress may not be as an important variable for NIDDM subjects for nondiabetic and IDDM subjects.

Conclusions and Future Research

In addition to direct means of affecting blood glucose levels (by the modification of diet, exercise, and medication), it is evident that psychological stress (via the autonomic nervous system) is important in the regulation of carbohydrate metabolism. However, there is not a simple, linear relationship between stress and blood glucose levels. Paradoxical findings regarding blood glucose levels during stress relates to the complex homeostatic regulation of blood glucose. Briefly, the glucose reducing effects of insulin are opposed by the action of glucagon, catecholamines, and cortisol. This process is affected differentially by the presence of IDDM and NIDDM. Superimposed on this regulatory mechanism are the effects of food intake, gastric motility, insulin (type, dosage, and time of administration), age, and carbohydrate metabolism, each of which may change blood glucose substantially.

All of the above factors contribute to the variability of the results in the literature. For example, the results of the present study may have been very different if there was a change in the placement of the stressor in relation to the glucose load. In a post-absorptive state, delayed gastric emptying under stress would not have the marked effect it has on blood glucose when the stress occurs just after a meal. Additionally, the availability of insulin at the time of the stressor is another extremely influential variable which would determine blood glucose direction. For example, a different effect would be expected for IDDM subjects if the stressor occurred before insulin administration or before the liquid meal. Perhaps IDDM and NIDDM glucose data would look more similar if insulin was withheld from the IDDM group the morning of the study.

These factors may explain the negative results found in the fairly recent, relatively well-designed studies assessing lab stress on IDDM subjects. Kemmer et al. (1986) and Edwards and Yates (1985) found no significant change in blood glucose reactivity to stress for IDDM subjects. These subjects took their usual morning doses of insulin at 6 a.m. and ate a standard meal at about 2 p.m. before beginning the stress induction procedure approximately 2 hours later. Perhaps the presence of a post-absorptive state and adequate insulin levels is optimal for blood glucose stability during stress and therefore does not disturb glycemic control.

However, Delameter et al. (1988) found similar results studying IDDM subjects in the morning after an overnight fast prior to insulin administration. Although subjects administered their regular insulin dose the night before and the morning of the experimental session, no information regarding meal times or study times were provided in the Gilbert et al. (1989) study. This possibly uncontrolled factor may have contributed to the variability of the results. Additionally, blood glucose was only measured twice, before and after the study. The lack of report of important variables (e.g., time of last meal, measurement of recent insulin dose) in addition to the extremely methodologically flawed designs prevented proper evaluation of stress effects in the early studies (e.g., Vandenbergh et al., 1966, 1967). It is obvious that future research varying the temporal placement of the stressor in relation to the last meal and the insulin injection is needed to clarify the nature of these influences. It appears that the stress effect may be much more prominent when it occurs immediately after a meal.

A study on normal subjects by Hamburg, Hendler, and Sherwin (1980) revealed that moderate increases in epinephrine infusion had minimal effect on fasting blood glucose, but had a very strong potentiating effect on blood glucose increase subsequent to a 100 gm oral glucose load. Levels of glucose increased by 30 to 60 mg/dl above saline

control values. These data suggest marked sensitivity to the insulin antagonistic effects of epinephrine. The researchers conclude that evidence suggests that epinephrine has its most powerful effect on insulin action (not insulin secretion) and especially insulin facilitated glucose uptake. In 1952, Hinkle and Wolf, noted that glucose ingestion in a diabetic patient already experiencing stress led to a glucose curve that is "higher and more prolonged than in the absence of stress."

In examining the relationship between stress and diabetes, the effects of possible modifying and mediating variables must be considered. Individual differences, both psychological and physiological (in addition to the insulin variable) may account for the variability in the impact of the stress. It is useful to consider individual differences in studies of stress reactivity since blood glucose increases and decreases would cancel each other out when combining group data, possibly obscuring specific stress effects in some patients. In a report of preliminary data, Carter, Gonder-Frederick, Cox, Clarke, and Scott (1985), found blood glucose changes with stress (mental arithmetic) to be idiosyncratic but reliable in a sample of adult IDDM subjects. Delameter and his colleagues' results (1988) support their observation, with a high consistency of blood glucose change observed across the three stress conditions. Thus it is possible that there are subgroups of patients for

whom stress is associated with different patterns of response. The reliability of individual patterns could have been assessed in the present study by adding a third study (stress) day to the experimental design. Of course the confounding variable of a habituation effect would have to be dealt with. A very important, relevant subgroup to study would be patients with autonomic neuropathy (screened out in the present study). Impairment in the stress hormone responses secondary to autonomic neuropathy, could interfere with epinephrine-induced increases in blood glucose. These patients may have a very different response to stress. Another important subgroups to study would be patients in good vs poor control.

Cardiovascular research has suggested that individuals with Type A behavior patterns may aggravate the endocrine response to stress. Although no consistent results were evident in past studies (Stabler, et al., 1988) additional research examining differential responses of Type A and Type B individuals may be interesting.

Along these lines, as discussed in the introduction, different types of stressors may have different effects on the neuroendocrine system and thus carbohydrate metabolism. Research utilizing different types of stressors (e.g., active versus passive) in the present design would be valuable. A design similar to the one proposed above (3 experimental days) using two different stressors in

counterbalanced order may provide a good start to assessing the potential differences.

The time course of metabolic changes in relationship to psychological stress and the strength of the stress response necessary to disrupt glucose metabolism has to be defined. For example, the fact that Delameter's study failed to show catecholamine increases in response to stress may account for the negative results. Further research varying the intensity and duration of the stressor is necessary. It would be very interesting to study whether a longer stressor (which is more generalizable to the natural environment) prolongs the delay in gastric emptying and accentuates the stress effects noted in each group. Perhaps the blood glucose curve would show prolonged hyperglycemia in the NIDDM group and a prolonged or steeper decrease in the IDDM group.

Meal composition is another variable which needs to be manipulated. High fiber foods which are digested more slowly than the liquid Sustacal are likely to affect the blood glucose curve differently. For example, a meal high in fiber may actually exaggerate the initial decrease in blood glucose noted in the IDDM subjects.

Another line of research involves identifying (or confirming) the mechanisms responsible for the various effects. Frequent sampling of indices of autonomic response (e.g., catecholamines, cortisol, glucagon) as well as

measures of gastric emptying should be included. Recent investigations utilizing a glucose/insulin infusion system allows greater control of baseline levels. Chemical infusion studies help demonstrate the direct effect of stress hormones on blood glucose and insulin.

Lastly, research assessing the external validity of these stress-induction studies is very important. Do the psychological and physiological effects of the lab stressors generalize to naturally occurring life events?

Implications

In addition to the numerous possible implications noted above, this study has several practical implications. The possible hypoglycemia and rebound observed in this study in response to stress may explain the difficulty controlling some IDDM patient's glucose levels during periods of stress. However, due to the high baseline levels of blood glucose, despite a precipitous drop during the stressor (up to 50 mg/dl), it was rare for a subject to actually attain a hypoglycemic level. One IDDM subject started at a blood glucose level of 74 mg/dl, dropped to approximately 56 mg/dl within the first 10 minutes of the stressor, and eventually "rebounded" to a level 25 mg/dl above baseline. An awareness of this potential to become hypoglycemic (particularly during a time when blood glucose levels are already low as in the above subject) may necessitate meal

changes (composition and timing) or insulin changes (dosage, type or timing). For example, in order to avoid a potential drop in blood glucose and subsequent rebound, an IDDM college student preparing for an early morning stressful exam, may want to eat breakfast before insulin administration to allow for some glucose absorption. A hypoglycemic episode would surely affect test performance or driving ability on the way to the test. Similarly, IDDM patients stressed 4-6 hours after insulin administration, when NPH peaks, may be more likely to experience a drop in blood glucose.

A disruption in regimen adherence due to life stress may potentiate the destablizing effects of stress on metabolic control. A behavior change (e.g., skipping a meal) combined with the phenomenon described in this study may prove to be dangerous for an IDDM individual.

Considering the effects of stress on NIDDM subjects, stress reduction techniques which decrease sympathetic nervous system activity may indeed have utility in the treatment of NIDDM particularly during periods of stress. The growing literature reporting the effects of relaxation training in NIDDM patients discussed earlier are promising.

Hopefully, the interesting results and discovery of crucial methodology revealed in the present study will help to end some of the frustration and motivate additional studies in this exciting research area in order to clarify

the role of psychological stress in diabetes control and ultimately enhance the health status of individuals with diabetes.

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APPENDIX A

Screening Questionnaire

SCREENING QUESTIONNAIRE

SH #:_____

DATE:_____

Name:_____ Sex: M F Age:_____ Birthdate_____

Address:_____ Home Ph#:_____

_____ Office Ph#:_____

Weight:_____ Height:_____

Years Education:_____

1. Do you smoke cigarettes?_____ If yes, would you be able to go without cigarettes from midnight till noon the next day?

2. Do you have Diabetes Mellitus?

   a) How long ago were you diagnosed?

   b) Do you consider yourself in good, fair, or poor control?

   c) Type 1 or Type 2?

   d) Insulin dependent or non-insulin dependent?

   If IDDM, what is your insulin type/dosage?

   If NIDDM, how do you control your diabetes, Explain.
   Oral agents? (Type and dose)

   Diet?

   Other?

3. If you do not have diabetes, do you have an immediate family history of diabetes? If yes, list.

4. Are you generally healthy? List any acute or chronic problems (particularly cardiovascular and neurological) including colds and flu.

5. Are you on any medications? List all meds and dosages.
   Fludrocortisone?
   Beta-adrenergic antagonists?
   Other hypertensive agents?
   Other medications?

6. Are you on a salt restricted diet?

7. Have you ever been diagnosed as having autonomic neuropathy?

   Do you have any of the following symptoms:
   Postural dizziness_____
   Gastrointestinal problems_____
   Erectile dysfunction (if male)___

8. Females: date of your last period?_____ How many days did it last?

9. Is there anything else about you (i.e., physically, psychologically) that this questionnaire doesn't cover that we should know about?

Results of Life Events Checklist:

Result of Ewing (R-R Interval) Test

APPENDIX B

ASSESSMENT OF DIABETIC NEUROPATHY VIA R-R INTERVAL PROCEDURE

Assessment of Diabetic Neuropathy

Cardiovascular reflexes maintain physiological homeostasis by reflecting the constant flux on demand imposed by external environmental influences. These reflexes are mediated via the autonomic nervous system. Thus, autonomic neuropathy in diabetes may have a profound effect in impeding or even eliminating the ability to respond appropriately to environmental demands. Classic signs include orthostatic hypotension, gastrointestinal symptom, and erectile dysfunction in males. Subjects with diabetic neuropathy were excluded from this study in order to control for the liklihood of an inconsistent response. The following R-R Interval procedure was used to test for the presence of diabetic neuropathy.

R-R Interval Procedure

The patient was instructed to lie quietly for at least 3 minutes and then stand up rapidly (within 5 seconds) and remain motionless for 2 minutes. Continuous electrocardiographic monitoring was occurring during this process. A 30:15 ratio (length of the R-R interval at beat 30 following standing divided by the length of the R-R interval at beat 15) was used as an index of appropriate heart rate increase. A ratio of less than 1.0 was taken as evidence of autonomic dysfunction.

APPENDIX C

SOCIAL READJUSTMENT RATING SCALE

Name:_____ Date:_____

Social Readjustment Rating Scale

Listed below are a series of life events. Circle any that have happened to you in the last month. Next to each event circled, indicate whether the event was primarily a **positive** (good) experience, or a **negative** (bad) experience. Rate only those events you circled.

	Events	Type of Events
1.	Marriage	positive...negative
2.	Troubles with the boss	positive...negative
3.	Detention in jail or other institution	positive...negative
4.	Death of spouse	positive...negative
5.	Major change in sleeping habits (a lot more, or a lot less sleep, or change in part of day when asleep	positive...negative
6.	Death of a close family member	positive...negative
7.	Major change in eating habits (a lot more, or a lot less food intake, or very different meal hours or surroundings)	positive...negative
8.	Foreclosure on a mortgage or loan	positive...negative
9.	Revision of personal habits (dress, manners, associations, etc.)	positive...negative
10.	Death of a close friend	positive...negative
11.	Minor violations of the law (e.g., traffic tickets, jay walking, disturbing the peace, etc.)	positive...negative
12.	Outstanding personal achievement	positive...negative
13.	Pregnancy	positive...negative
14.	Major change in the health or behavior of a family member	positive...negative
15.	Sexual difficulties	positive...negative
16.	In-law troubles	positive...negative

Social Readjustment Scale
page 2

17. Major change in number of family get-togethers (e.g, a lot more or a lot less than usual) . . . . . **positive...negative**

18. Major change in financial state (e.g., a lot worse off, or a lot better off than usual) . . . . . **positive...negative**

19. Gaining a new family member (e.g., through birth, adoption, oldster moving in, etc.) . . . . . **positive...negative**

20. Change in residence . . . . . **positive...negative**

21. Son or daughter leaving home (e.g., marriage, attending college, etc.) . **positive...negative**

22. Marital separation from mate . . . . . **positive...negative**

23. Major change in church activities (e.g., a lot more or a lot less than usual) . . . . . **positive...negative**

24. Marital reconciliation with mate . . . . . **positive...negative**

25. Being fired from work . . . . . **positive...negative**

26. Divorce . . . . . **positive...negative**

27. Changing to a different line of work . . . . . **positive...negative**

28. Major change in the number of arguments with spouse (e.g., either a lot more or a lot less than usual regarding child-rearing, personal habits, etc.) . . . . . **positive...negative**

29. Major change in responsibilities at work (e.g., promotion, demotion, lateral transfer) . . . . . **positive...negative**

30. Wife beginning or ceasing work outside the home . . . . . **positive...negative**

31. Major change in working hours or conditions . . . . . **positive...negative**

32. Major change in usual type and/or amount of recreation . . . . . **positive...negative**

33. Taking on a mortgage or loan greater than $10,000 (e.g., purchasing a home, business, etc.) . . . . . **positive...negative**

34. Taking on a mortgage or loan less than $10,000 (e.g., purchasing a car, TV, freezer, etc.) . . . . . **positive...negative**

35. Major personal injury or illness . . . . . **positive...negative**

36. Major business readjustment (e.g., merger, reorganization, bankruptcy, etc.) . . . . . **positive...negative**

37. Major change in social activities (e.g., clubs, dancing, movies, visiting, etc.) . . . . . **positive...negative**

38. Major change in living conditions (e.g., building a new home, remodeling, deterioration of home or neighborhood) . . . . . **positive...negative**

39. Retirement from work . . . . . **positive...negative**

40. Vacation . . . . . **positive...negative**

41. Christmas . . . . . **positive...negative**

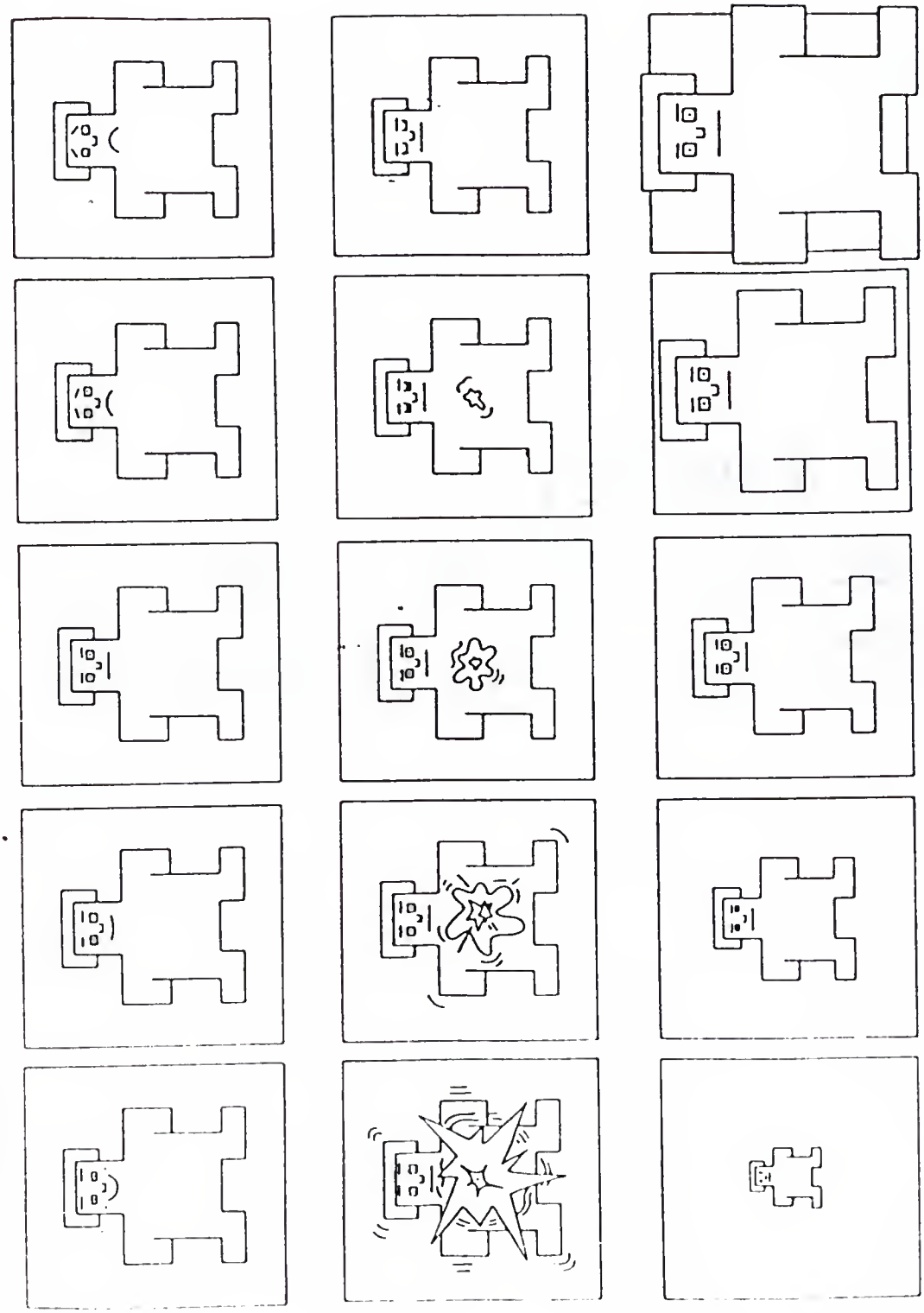
42. Changing to a new school . . . . . **positive...negative**

43. Beginning or ceasing formal schooling . . . . . **positive...negative**

APPENDIX D

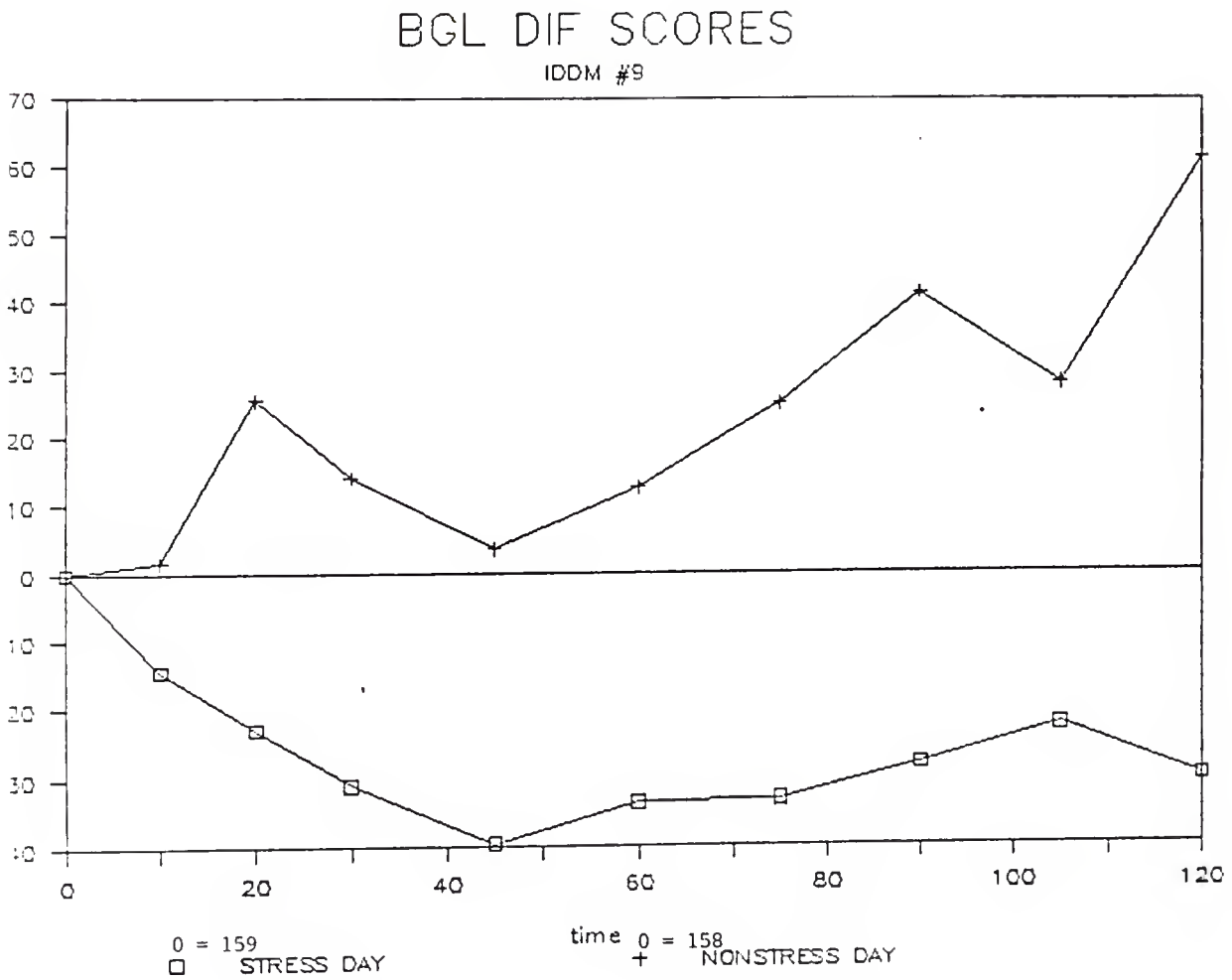
SELF-ASSESSMENT MANIKIN

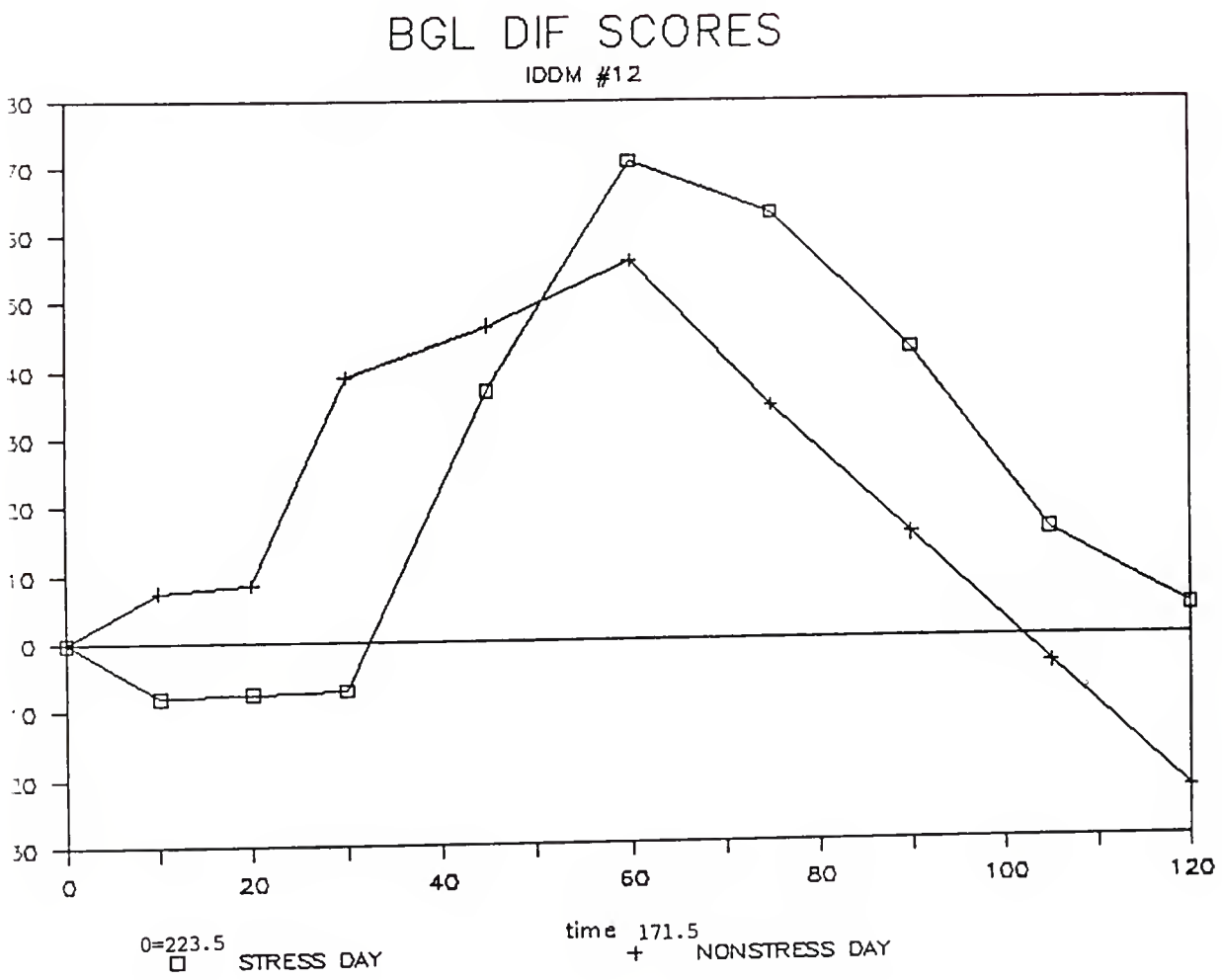
(SAM)



APPENDIX E

IDDM AND NIDDM SUBJECT GRAPHS


BGL DIF SCORES
IDDM #9
70
60
50
40
30
20
10
0
10
20
30
40
0
20
40
60
80
100
120
time
0 = 159
STRESS DAY
0 = 158
NONSTRESS DAY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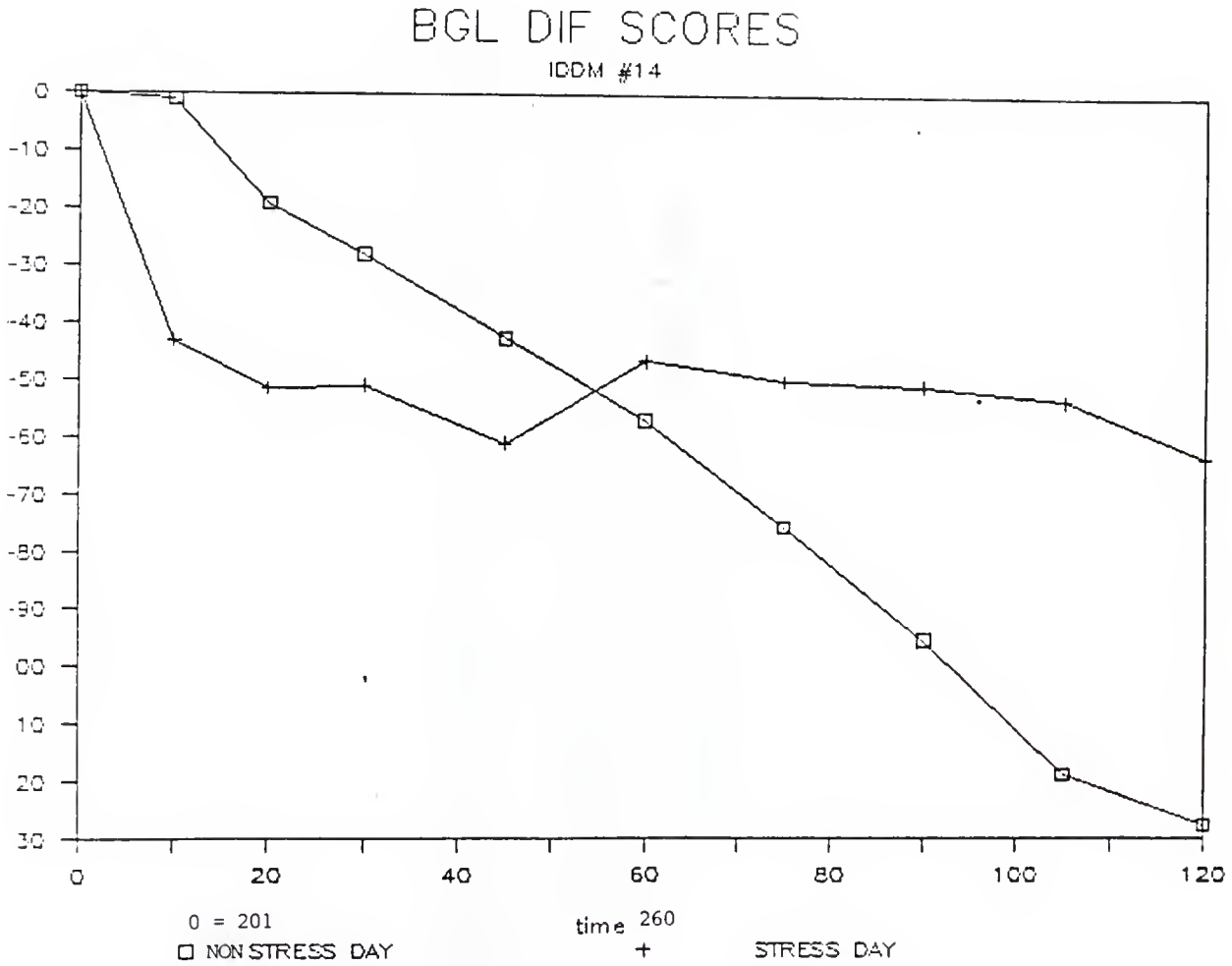
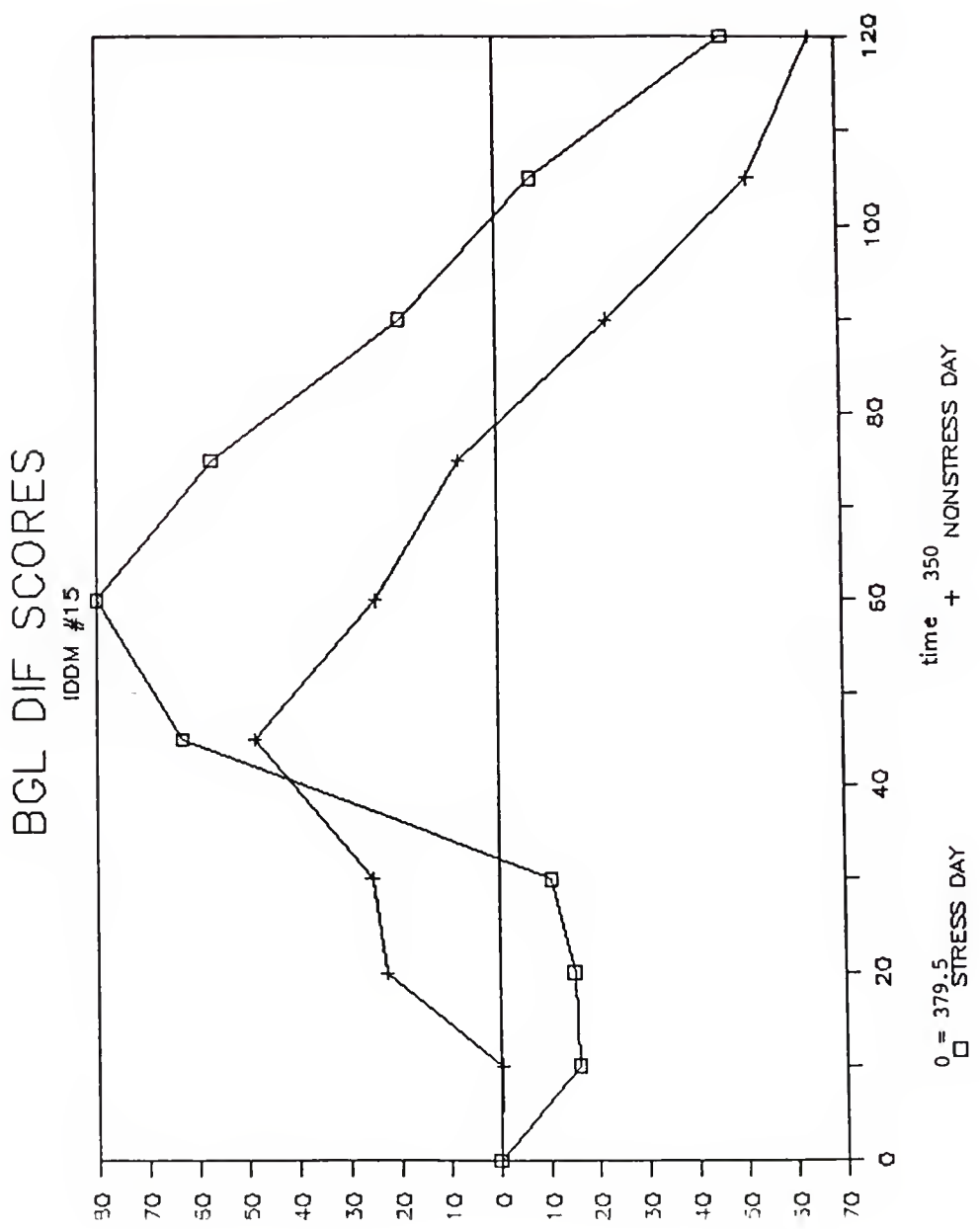
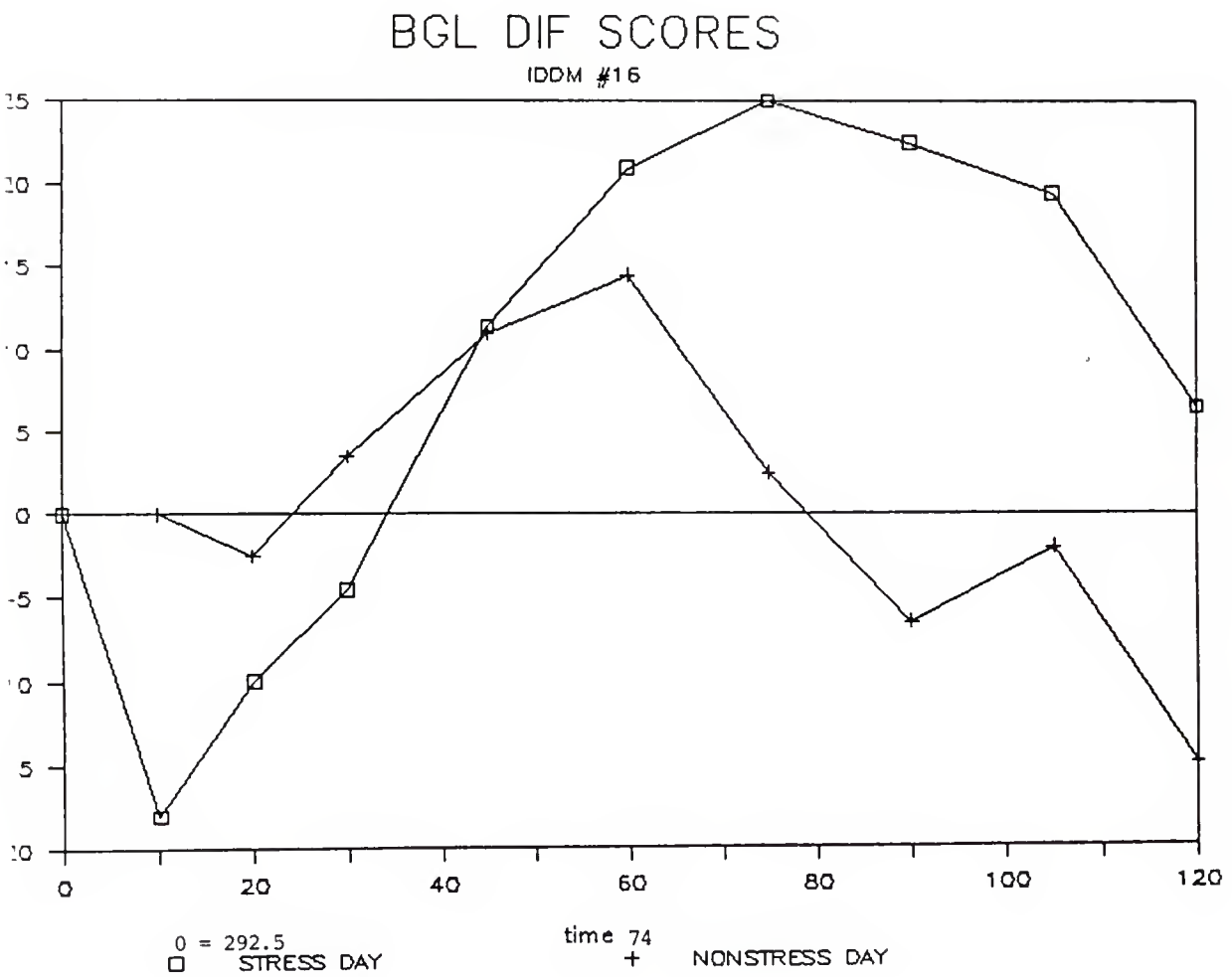
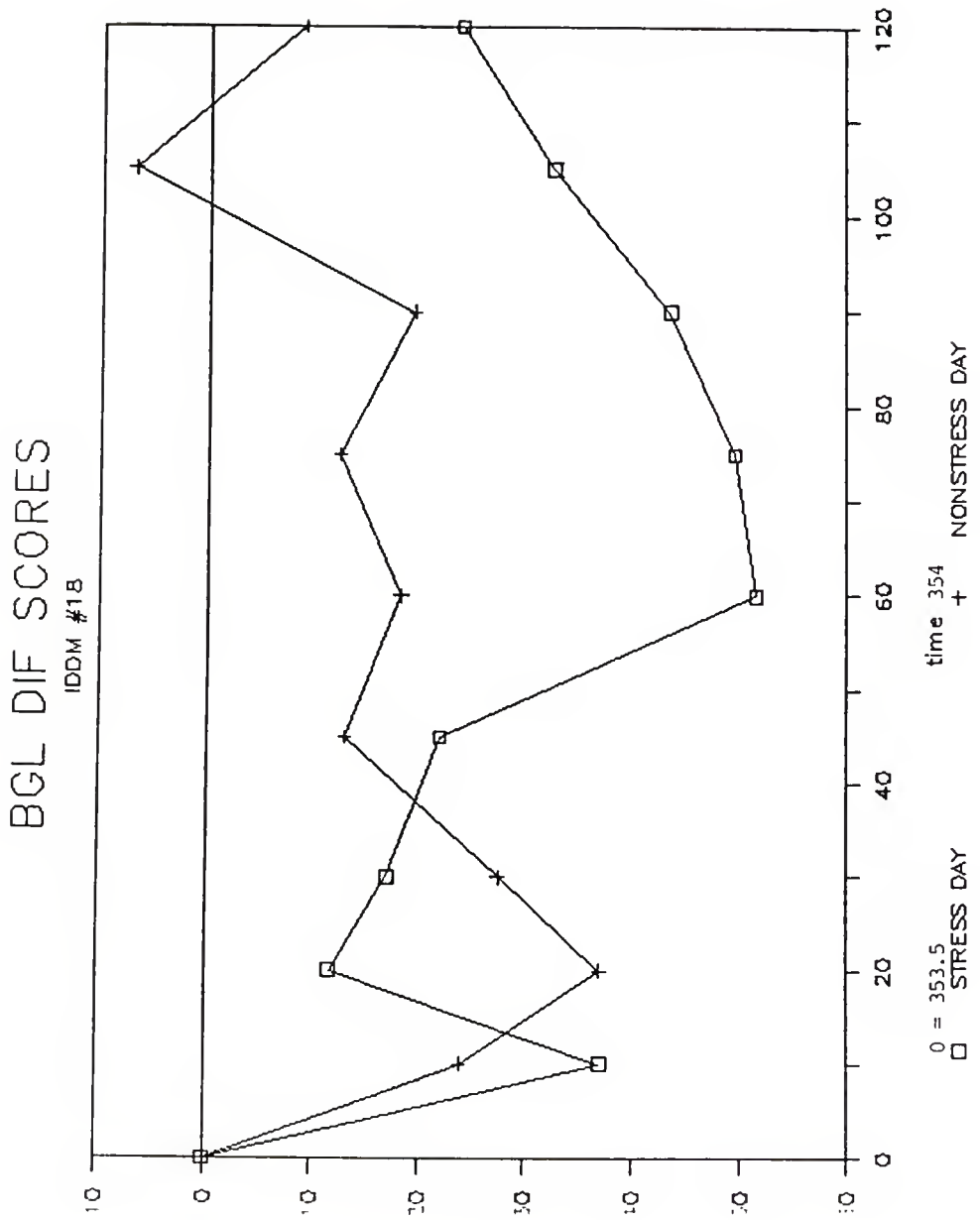
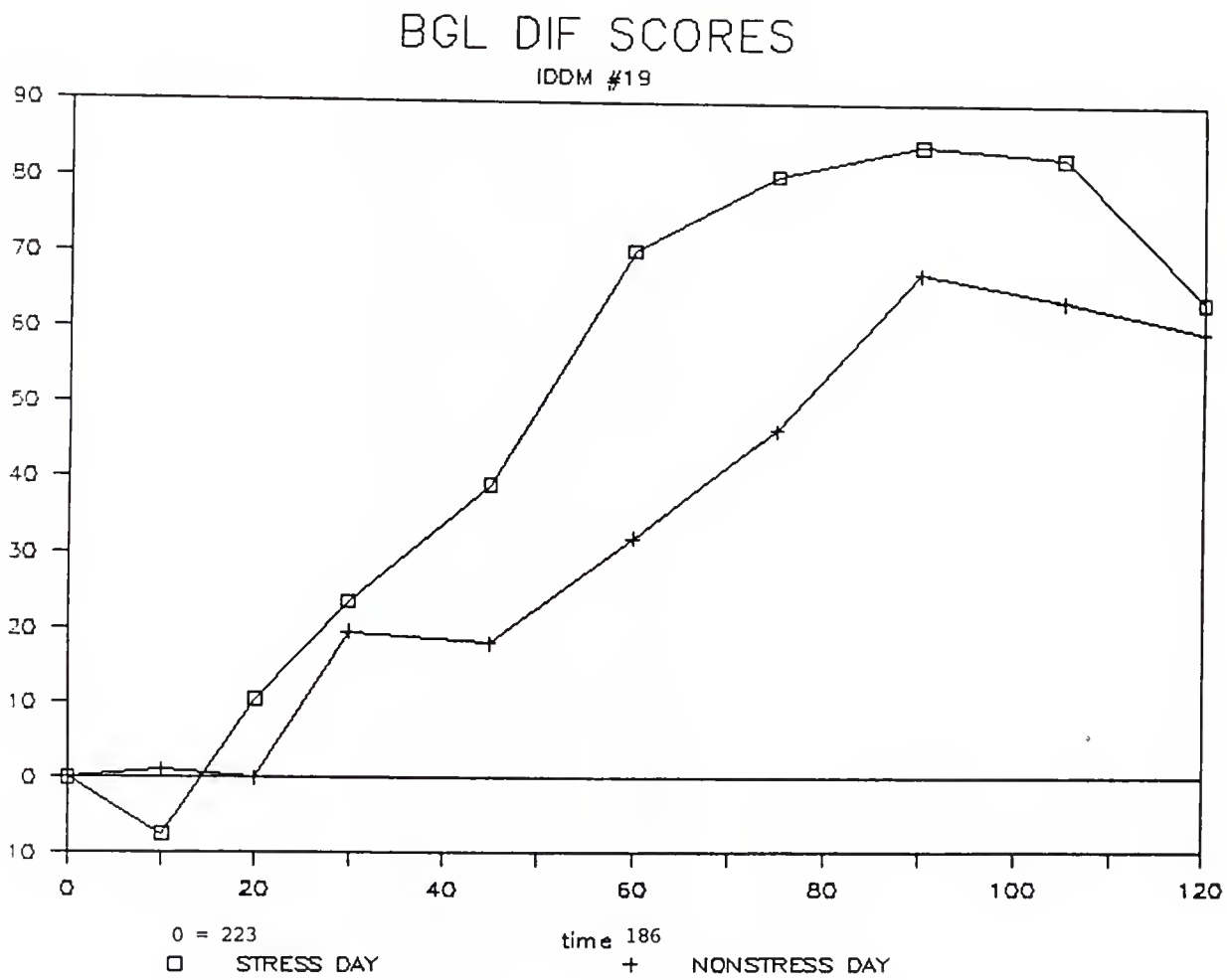
IDDM #12
30
70
30
50
40
30
20
10
0
10
20
30
0
20
40
60
80
100
120
time
0=223.5
STRESS DAY
171.5
+
NONSTRESS DAY

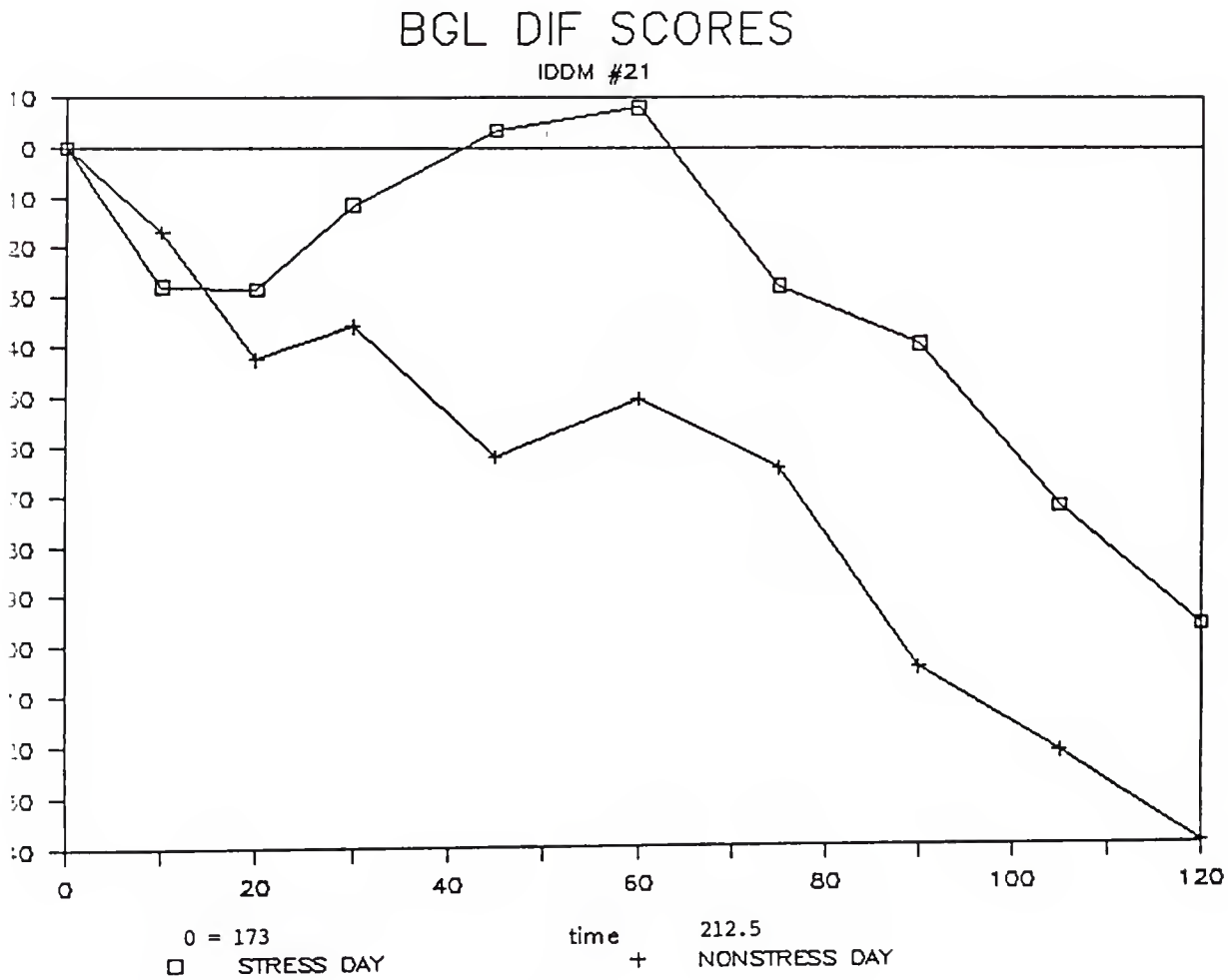

BGL DIF SCORES
IDDM #14
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
00
10
20
30
0
20
40
60
80
100
120
0 = 201
time 260
NON STRESS DAY
STRESS DAY

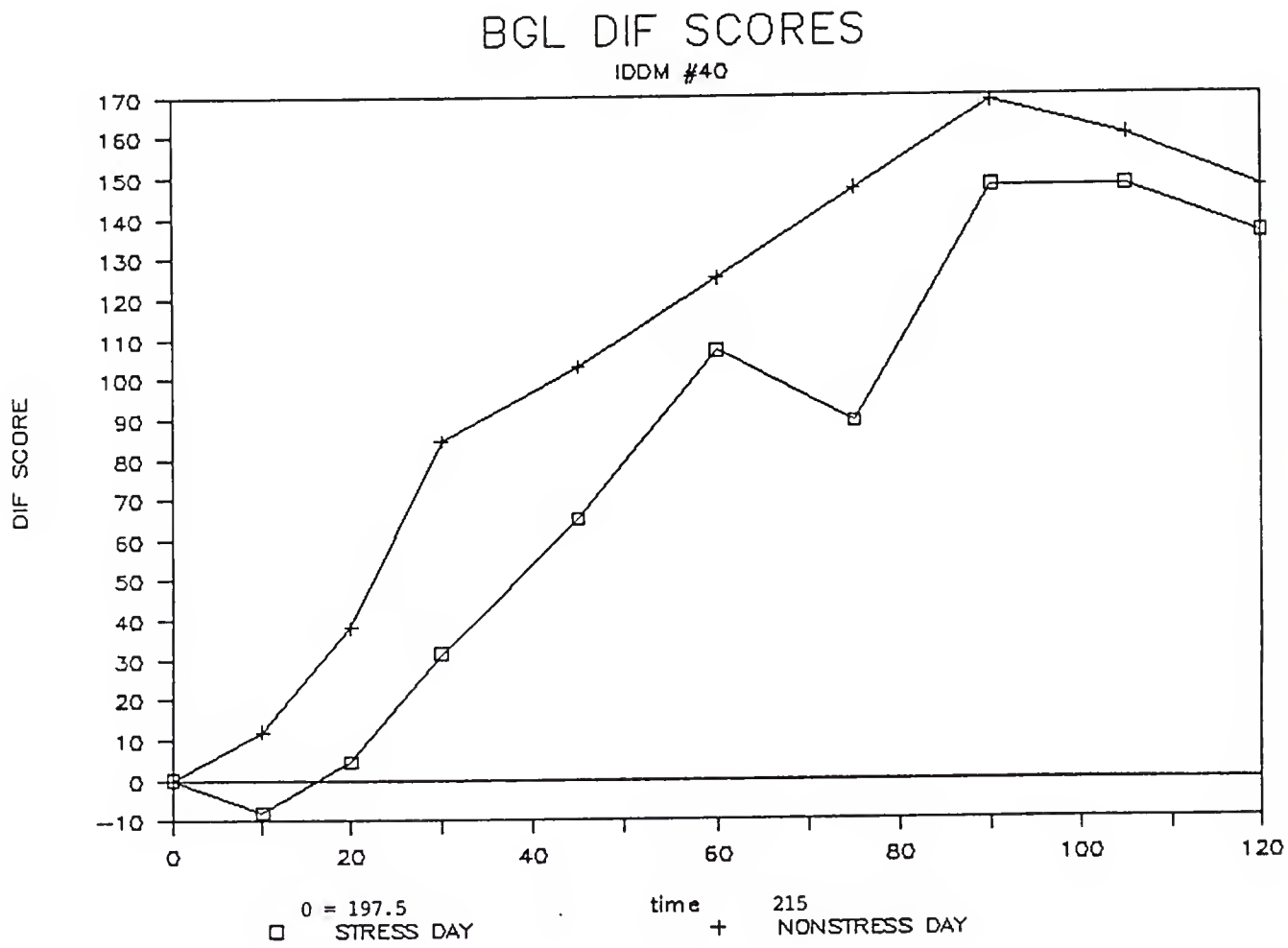

BGL DIF SCORES
IDDM #15
time
0 = 379.5 STRESS DAY
+ 350 NONSTRESS DAY
0
20
40
60
80
100
120
70
60
50
40
30
20
10
0
10
20
30
40
50
70

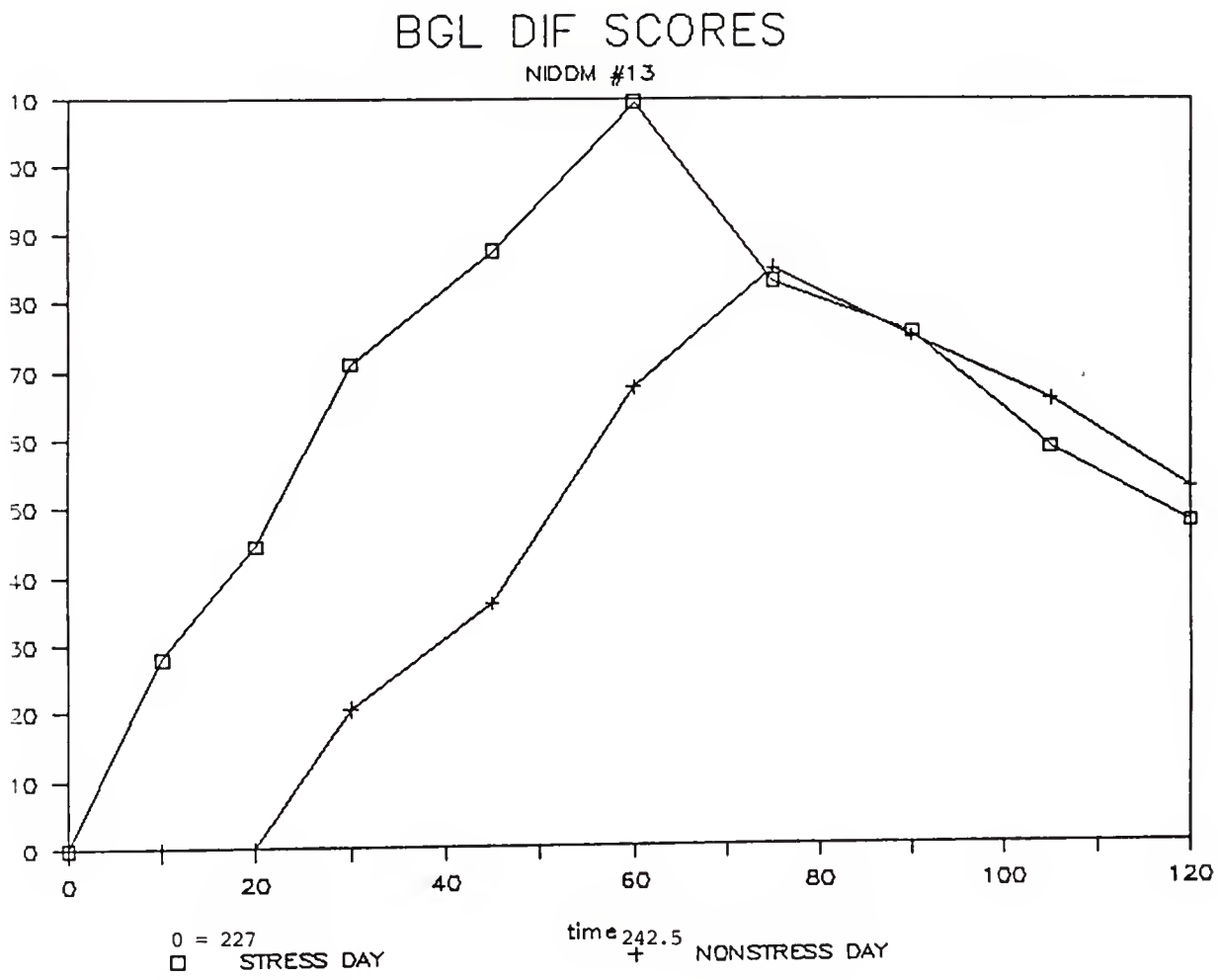

BGL DIF SCORES
IDDM #16
15
10
5
0
5
0
-5
0
5
10
0
20
40
60
80
100
120
time 74
0 = 292.5
STRESS DAY
NONSTRESS DAY

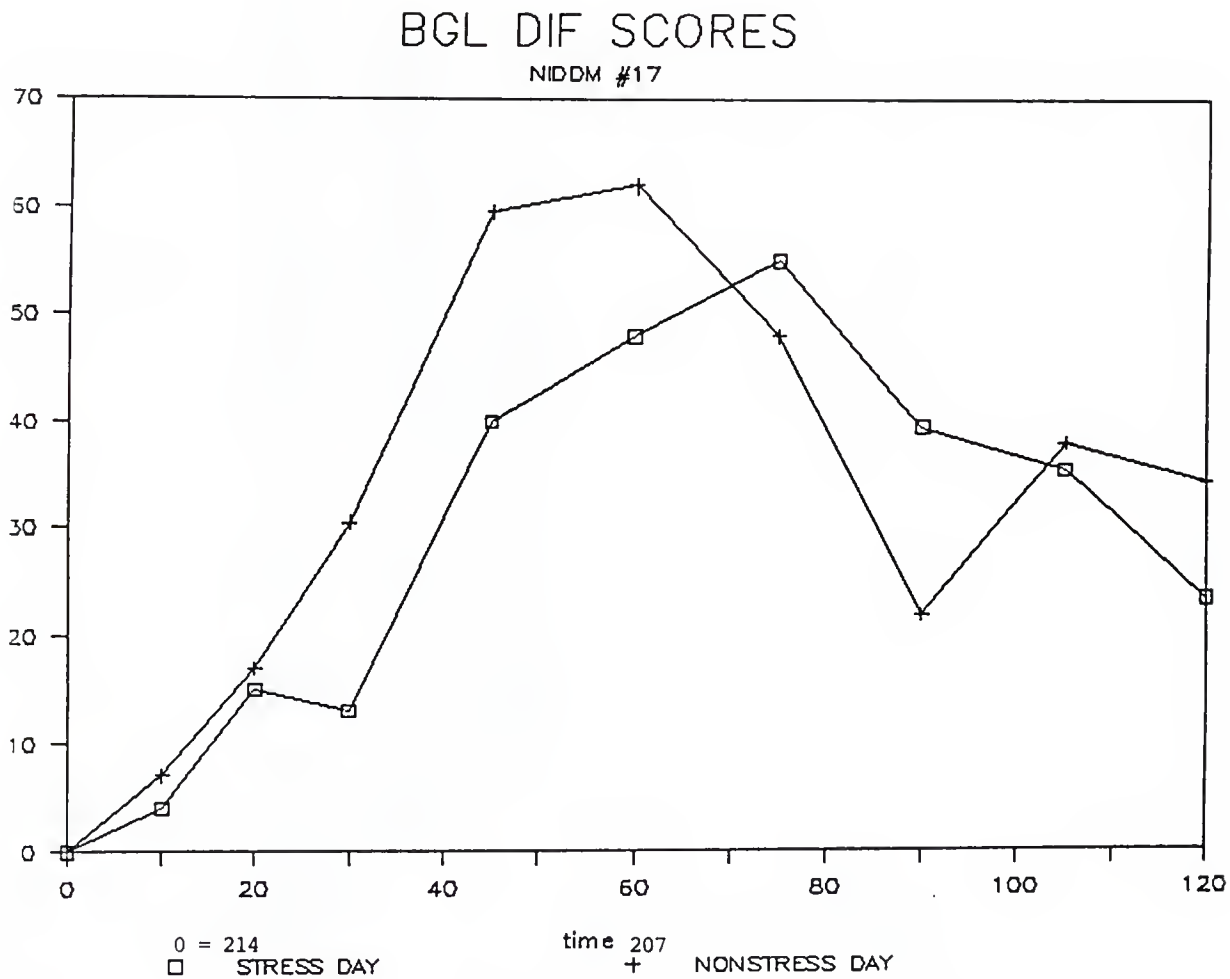

BGL DIF SCORES
IDDM #18
0
20
40
60
80
100
120
time 354
0 = 353.5 STRESS DAY
+ NONSTRESS DAY

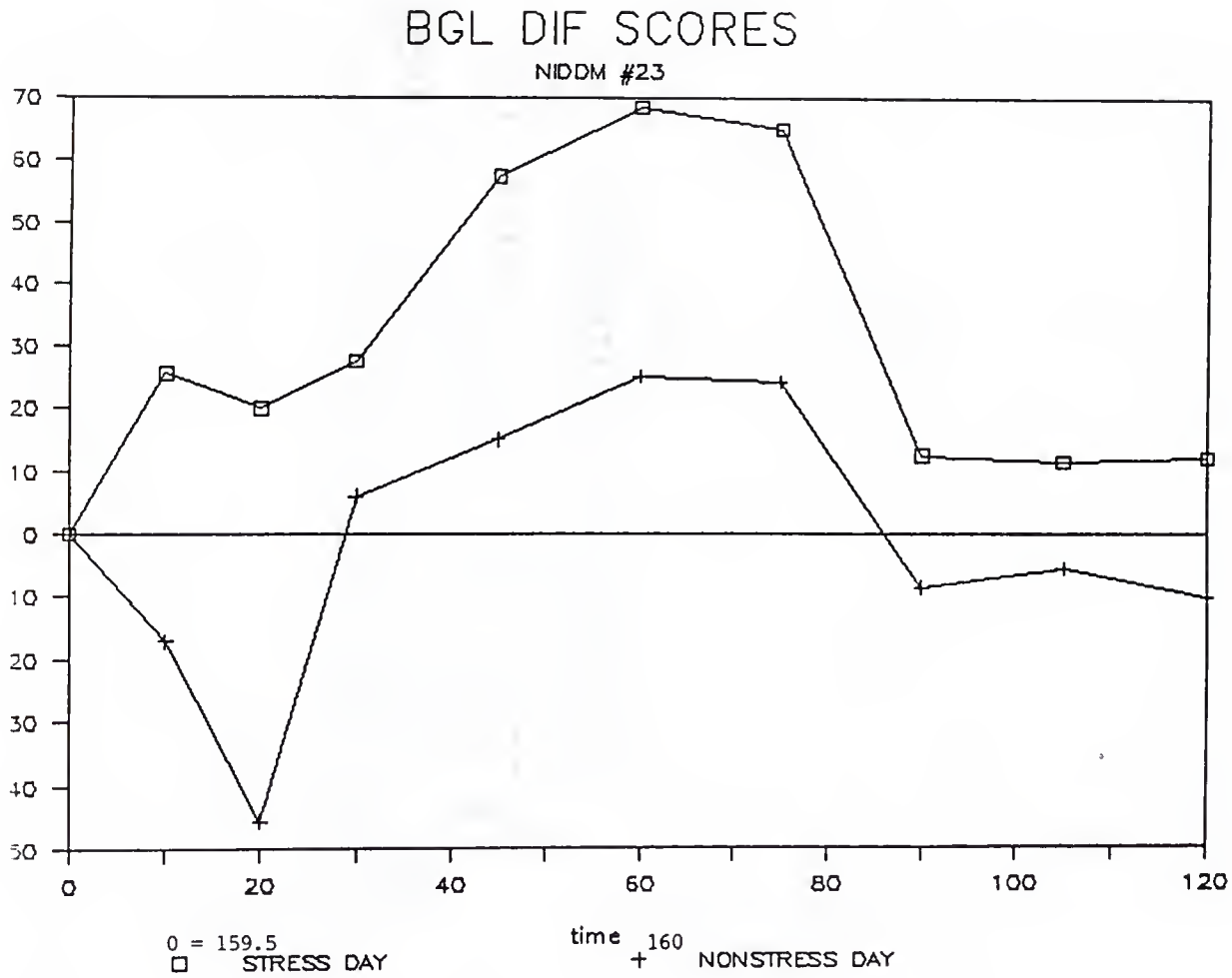

BGL DIF SCORES
IDDM #19
90
80
70
60
50
40
30
20
10
0
10
0
20
40
60
80
100
120
0 = 223
time 186
STRESS DAY
NONSTRESS DAY

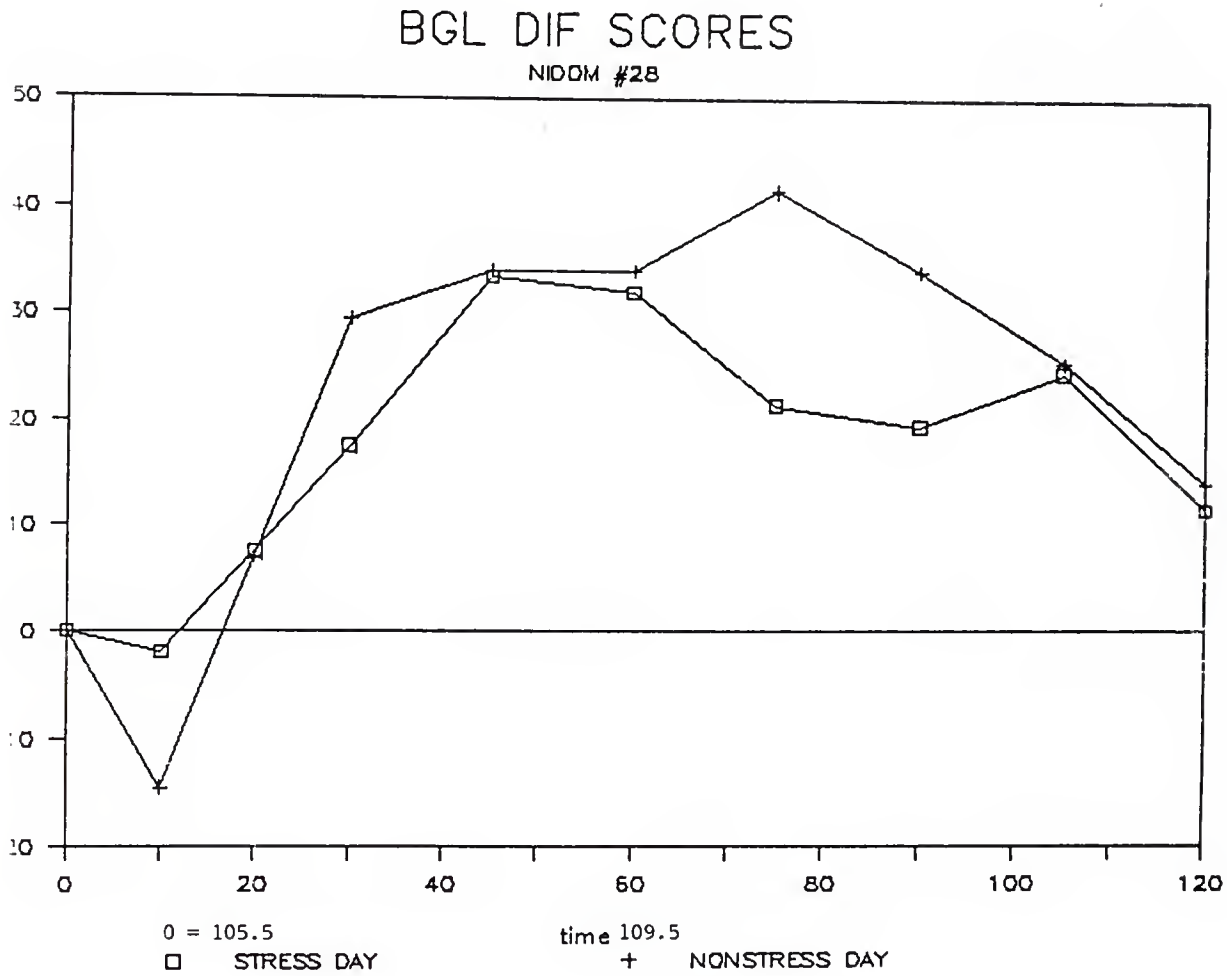

BGL DIF SCORES
IDDM #21
10
0
10
20
30
40
50
60
70
80
90
100
110
120
0
20
40
60
80
100
120
0 = 173
time
212.5
STRESS DAY
NONSTRESS DAY

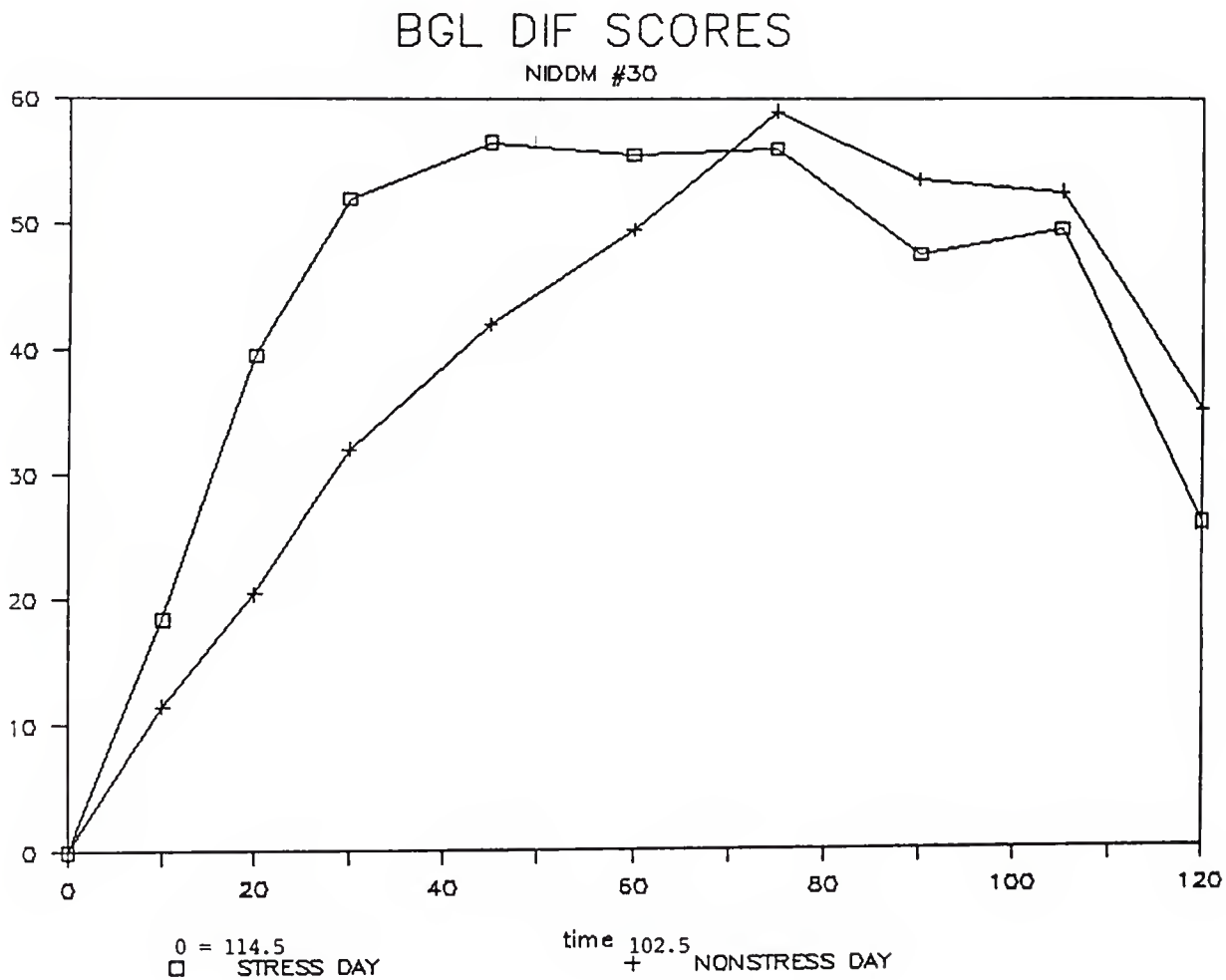

BGL DIF SCORES
IDDM #40
DIF SCORE
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
0
20
40
60
80
100
120
time
0 = 197.5
STRESS DAY
215
NONSTRESS DAY

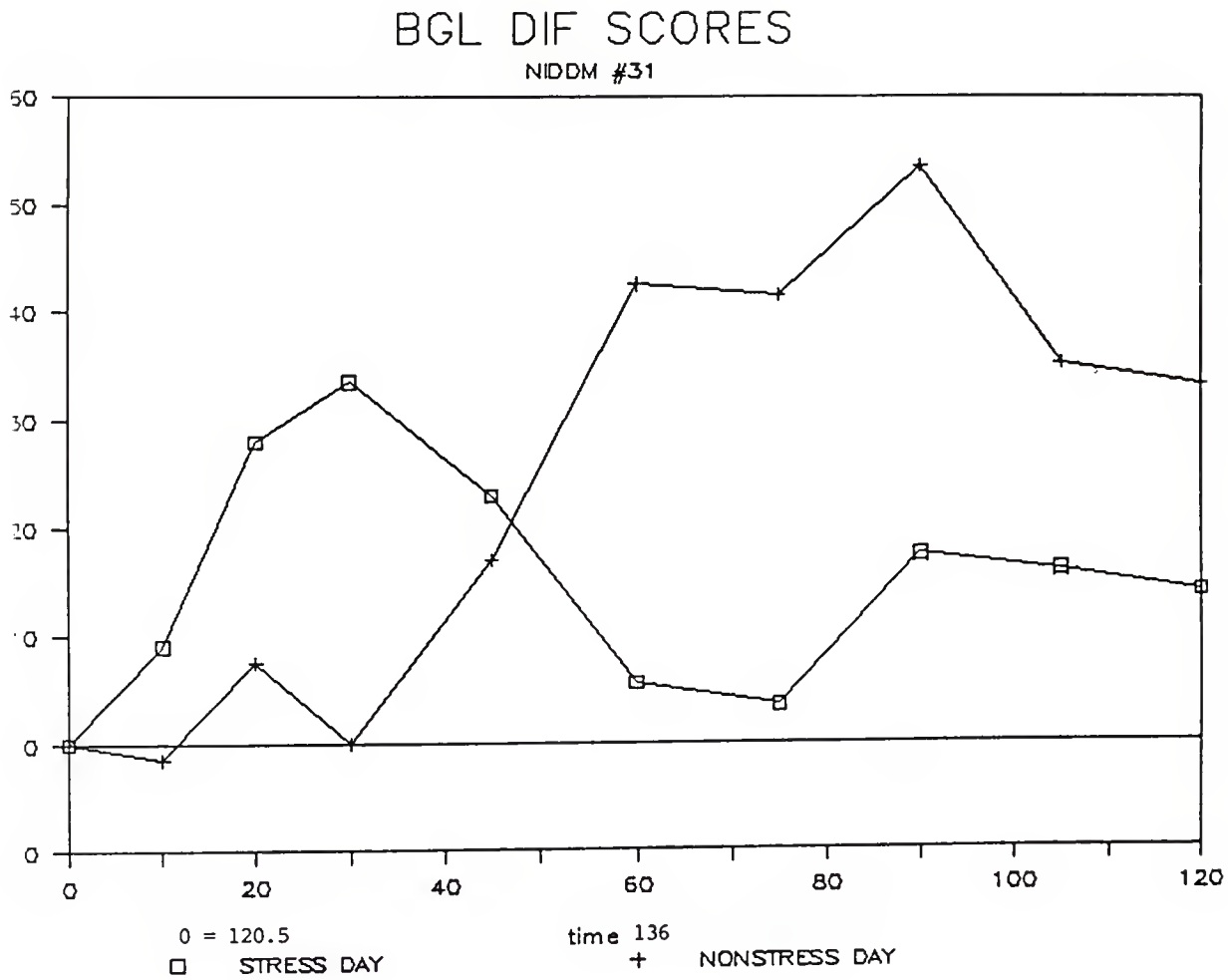

BGL DIF SCORES
NIDDM #13
10
30
90
80
70
60
50
40
30
20
10
0
0
20
40
60
80
100
120
time
0 = 227
STRESS DAY
242.5
NONSTRESS DAY

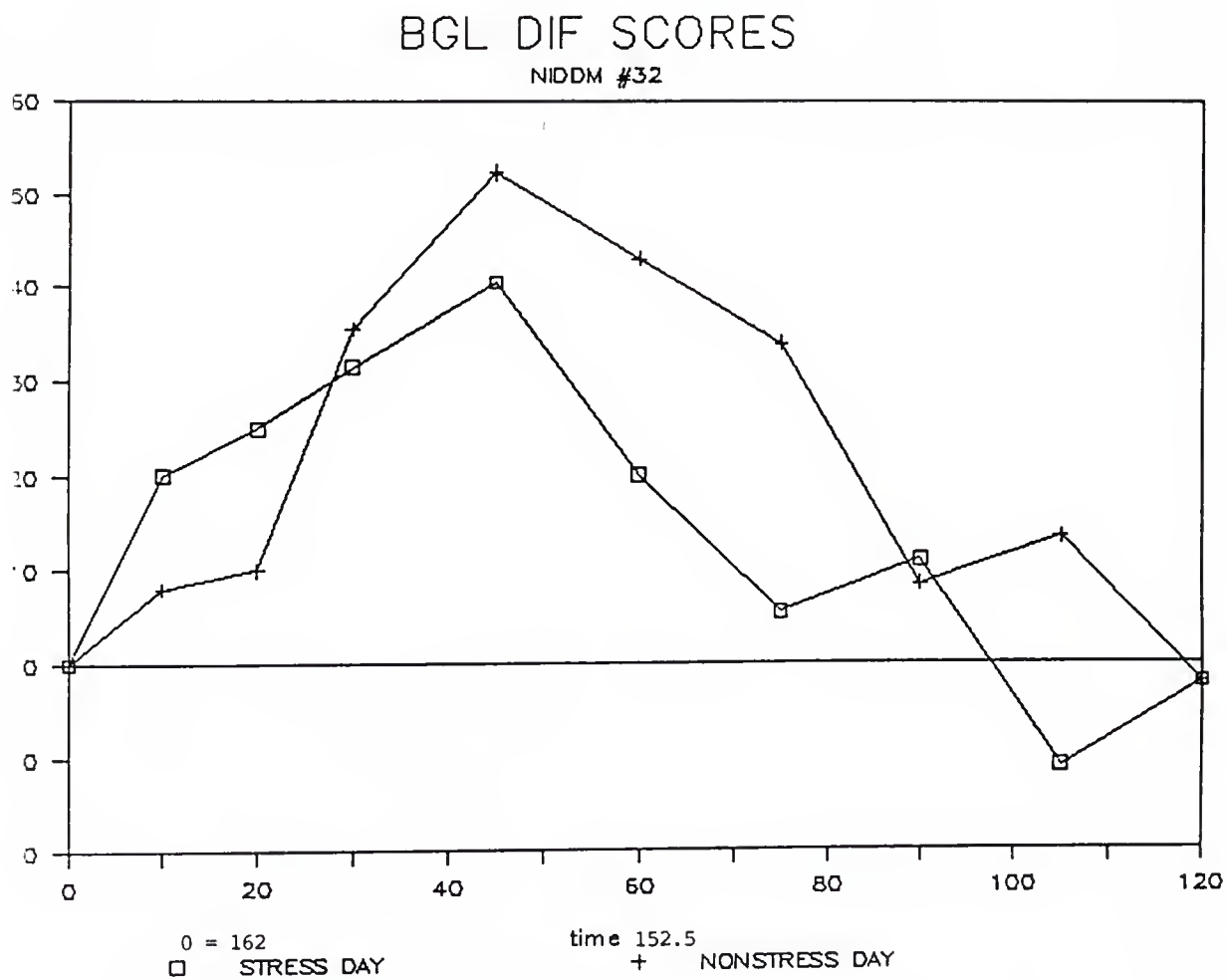

BGL DIF SCORES
NIDDM #17
70
60
50
40
30
20
10
0
0
20
40
60
80
100
120
time
0 = 214
STRESS DAY
207
NONSTRESS DAY


BGL DIF SCORES
NIDDM #23
70
60
50
40
30
20
10
0
10
20
30
40
50
0
20
40
60
80
100
120
time
0 = 159.5
STRESS DAY
160
NONSTRESS DAY


BGL DIF SCORES
NIDDM #28
50
40
30
20
10
0
10
20
0
20
40
60
80
100
120
0 = 105.5
time 109.5
STRESS DAY
NONSTRESS DAY


BGL DIF SCORES
NIDDM #30
60
50
40
30
20
10
0
0
20
40
60
80
100
120
time
0 = 114.5
STRESS DAY
102.5
NONSTRESS DAY


BGL DIF SCORES
NIDDM #31
50
50
40
30
10
0
0
0
0
20
40
60
80
100
120
0 = 120.5
time 136
STRESS DAY
NONSTRESS DAY


BGL DIF SCORES
NIDDM #32
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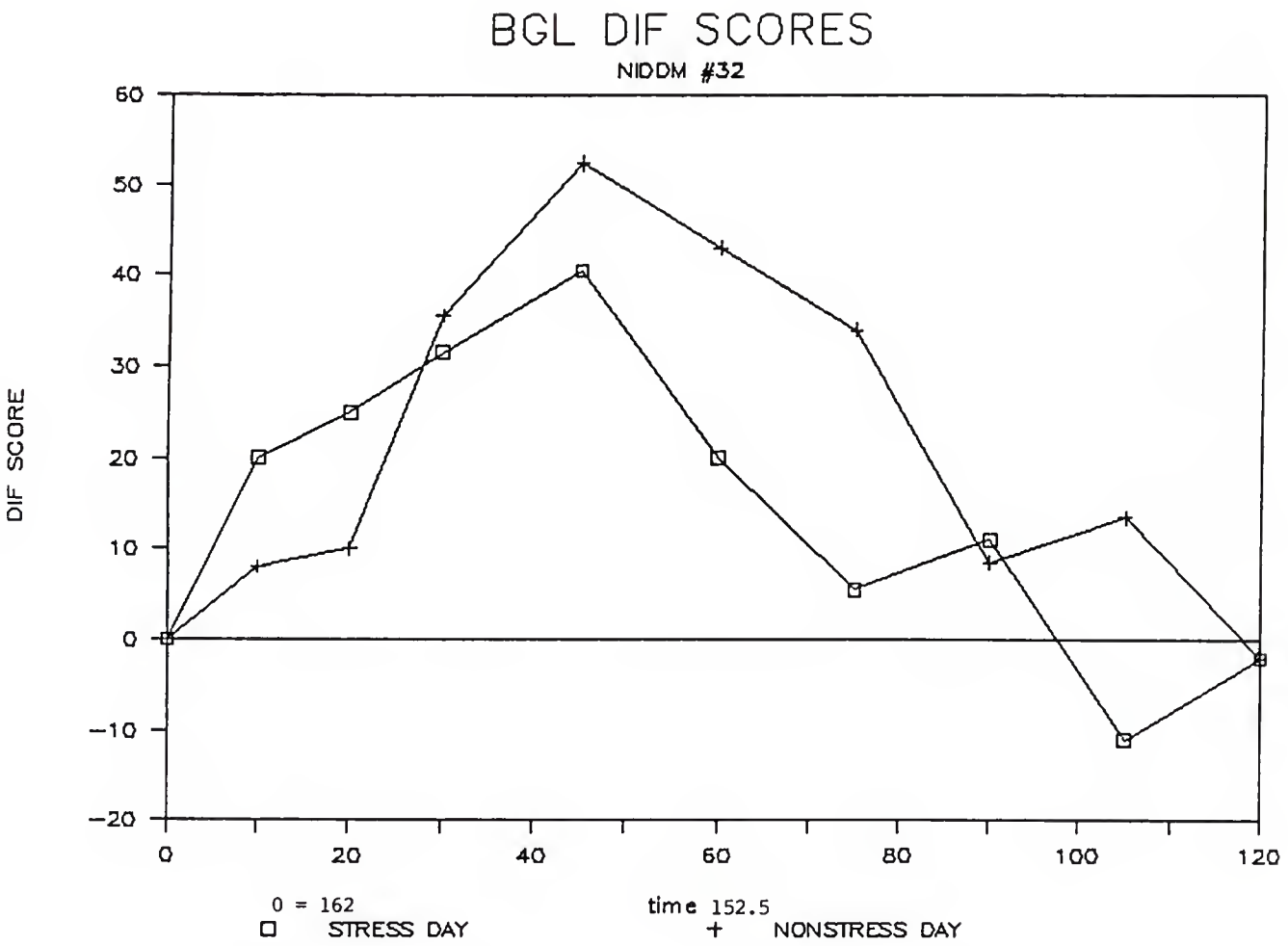
50
40
30
20
10
0
0
0
0
20
40
60
80
100
120
0 = 162
time 152.5
STRESS DAY
NONSTRESS DAY


BGL DIF SCORES
NIDDM #32
DIF SCORE
60
50
40
30
20
10
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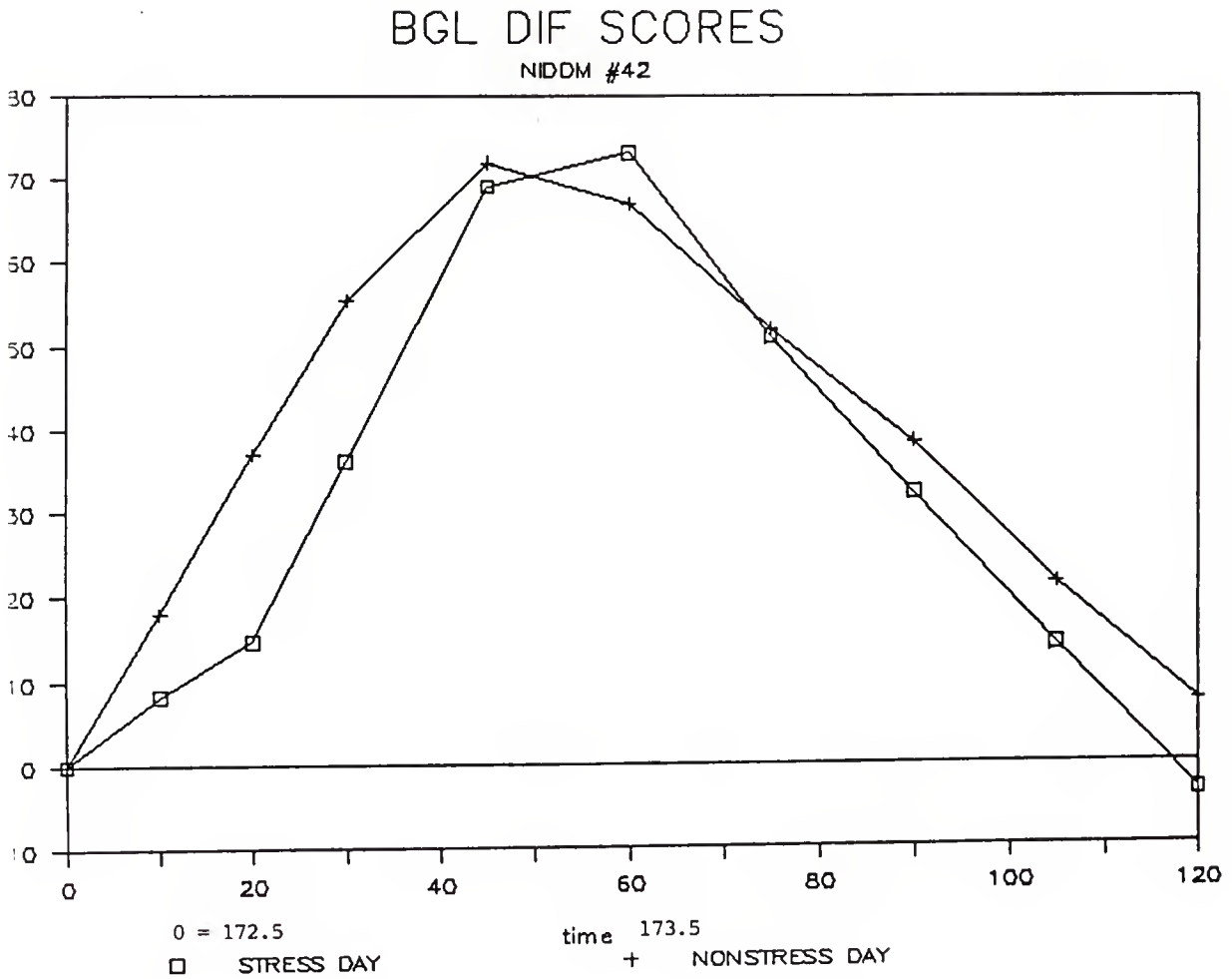
-10
-20
0
20
40
60
80
100
120
0 = 162
time 152.5
STRESS DAY
NONSTRESS DAY


BGL DIF SCORES
NIDDM #42
80
70
60
50
40
30
20
10
0
10
0
20
40
60
80
100
120
0 = 172.5
time 173.5
STRESS DAY
NONSTRESS DAY

BIOGRAPHICAL SKETCH

Jill A. Samo was born and raised in West Orange, New Jersey. After moving to South Florida at the age of 14 with her family, she attended high school at Pine Crest Preparatory School in Fort Lauderdale. She went to college at the University of Florida and enjoyed it so much she stayed for Graduate School. Her internship year was spent in Charleston, South Carolina, at the Medical University of South Carolina. She is currently working as a psychologist in New Jersey.

I certify that I have read this study and that in my opinion it conforms to acceptable standards of scholarly presentation and is fully adequate, in scope and quality, as a dissertation for the degree of Doctor of Philosophy.

Suzanne Bennett Johnson, Chair
Professor of Clinical and Health Psychology

I certify that I have read this study and that in my opinion it conforms to acceptable standards of scholarly presentation and is fully adequate, in scope and quality, as a dissertation for the degree of Doctor of Philosophy.

Gary Geffken
Associate Professor of Clinical and Health Psychology

I certify that I have read this study and that in my opinion it conforms to acceptable standards of scholarly presentation and is fully adequate, in scope and quality, as a dissertation for the degree of Doctor of Philosophy.

Janet Silverstein
Associate Professor of Clinical and Health Psychology

I certify that I have read this study and that in my opinion it conforms to acceptable standards of scholarly presentation and is fully adequate, in scope and quality, as a dissertation for the degree of Doctor of Philosophy.

Frederick T. Murray
Professor of Exercise and Sport Sciences

I certify that I have read this study and that in my opinion it conforms to acceptable standards of scholarly presentation and is fully adequate, in scope and quality, as a dissertation for the degree of Doctor of Philosophy.

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I certify that I have read this study and that in my opinion it conforms to acceptable standards of scholarly presentation and is fully adequate, in scope and quality, as a dissertation for the degree of Doctor of Philosophy.

Hugh Davis
Professor of Clinical and Health Psychology

I certify that I have read this study and that in my opinion it conforms to acceptable standards of scholarly presentation and is fully adequate, in scope and quality, as a dissertation for the degree of Doctor of Philosophy.

James R. Rodrigue
Assistant Professor of Clinical and Health Psychology

This dissertation was submitted to the Graduate Faculty of the College of Health Related Professions and to the Graduate School and was accepted as partial fulfillment of the requirements for the degree of Doctor of Philosophy.

August, 1990

Dean, College of Health Related Professions

Dean, Graduate School

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